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Charles James Fox, M. D.
HARTFORD, CONN.

TRANSACTIONS OF THE

SECTION ON

Practice of Medicine

of the
American Medical Association
at the Sixty-First Annual
Session, held at St. Louis,
Mo., June 7 to 10, 1910

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LIST OF OFFICERS

Those named below have served as officers in this section. This section has included other subjects in the earlier years, as will be seen by the headings which denote the different section titles. The names of the officers have been taken from the published records, which are deficient in some cases. It will be appreciated if any additional data are brought to the attention of the Secretary of the American Medical Association.

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PROCEEDINGS OF THE SESSION

Tuesday, June 7—Afternoon

The Section was called to order by the Chairman, Dr. George Blumer, New Haven, Conn., at 2 p. m., in the Third Baptist Church.

Dr. Max Einhorn, New York, read a paper on "Experiences with the Duodenal Contents in Man." No discussion.

Drs. Harvey G. Beck and William Royal Stokes, Baltimore, read a paper on: "A Case of Diffuse Ventriculo-Septal Myocarditis with Adams-Stokes' Syndrome."

Dr. Isaac I. Lemann, New Orleans, read a paper on "A Study of a Case of Heart-Block with Auricular Alternating Pulse."

These two papers were discussed by Drs. Haven Emerson, New York, and Albert E. Taussig, St. Louis.

Dr. Seale Harris, Mobile, Ala., read a paper on "The Radical Cure of Malaria; Its Importance and How It May Be Attained." Discussed by Drs. Charles MacLellan, Chicago; Arnold Traubitz, Neelysville, Mo.; W. E. Chapman, Sheboygan, Mich.; I. J. Wolf, Kansas City, Mo.; Vernon Blythe, Paducah, Ky.; S. P. Child, Kansas City, Mo.; C. C. Bass, New Orleans; Joseph H. Pratt, Boston; G. C. Smith, Boston; J. A. Witherspoon, Nashville, Tenn.; C. Shattinger, St. Louis; R. Alexander Bate, Louisville, Ky.; Arthur C. Bell, Dallas, Tex.; I. I. Lemann, New Orleans; B. W. Fontaine, Memphis, Tenn.; J. A. Chilton, Van Buren, Mo.; T. J. Ragsdale, Lees Summit, Mo.; D. C. Walt, Little Rock, Ark.; A. H. Vandivert, St. Joseph, Mo.; A. Comings Griffith, Kansas City, Mo.; and Seale Harris, Mobile, Ala.

Dr. W. J. Calvert, Dallas, Tex., read a paper on "A Possible Differential Sign Between Cardiac Dilatation and Pericarditis with Effusion." Discussed by Drs. Haven Emerson, New York, and W. J. Calvert, Dallas, Tex.

Wednesday, June 8—Morning

The Section held a joint meeting with the Section on Pharmacology and Therapeutics at the Third Baptist Church.

The Chairman of the Section on Practice of Medicine, Dr. George Blumer, New Haven, Conn., called the meeting to order at 9:30 a. m.

The following four papers were read and discussed as a Symposium on the Circulatory Disorders in Acute Infectious Diseases:

Dr. W. G. MacCallum, New York: "Pathologic Physiology of the Circulatory Failure of Acute Infectious Disease."

Dr. George Dock, New Orleans: "Treatment of the Circulatory Failure of Acute Infectious Diseases with Drugs Other than Alcohol."

Dr. Joseph L. Miller, Chicago: "The Physiologic Action, Uses and Abuses of Alcohol in the Circulatory Disturbances of Acute Infection."

Dr. A. N. Richards, Chicago: "The Action of Alcohol on the Mammalian Heart."

These four papers were discussed by Drs. A. S. Loevenhart, Madison, Wis.; R. C. Cabot, Boston; DeLancey Rochester, Buffalo, N. Y.; J. A. Lichty, Pittsburg; Haven Emerson, New York; G. C. Smith, Boston; A. T. Livingston, Jamestown, N. Y.; G. W. McCaskey, Fort Wayne, Ind.; C. F. Hoover, Cleveland; A. Jacobi, New York; Lawrence Litchfield, Pittsburg; Frank A. Jones, Memphis, Tenn.; B. C. Walt, Little Rock, Ark.; George Dock, New Orleans, and J. L. Miller, Chicago.

This ended the joint meeting.

Dr. Lewis A. Conner, New York, read a paper entitled, "The Visceral Anesthesia of Tabes Dorsalis in Relation to the Diagnosis of Acute Inflammatory Conditions in the Abdomen, with an Illustrative Case." Discussed by Drs. L. Litchfield, Pittsburg; J. H. Musser, Philadelphia; C. F. Hoover, Cleveland, and Lewis A. Conner.

Wednesday, June 8—Afternoon

Dr. Richard C. Cabot, Boston, delivered the Oration on Medicine, entitled, "A Study of Mistaken Diagnoses Based on the Autopsy Findings in One Thousand Cases."

The Chairman announced that the following would serve on the Nominating Committee: Drs. George Dock, New Orleans; Seale Harris, Mobile, Ala., and Horace D. Arnold, Boston.

Dr. William F. Boos, Boston, read a paper on "Magnesium Poisoning: A Study of Ten Cases." Discussed by Drs. P. S. Roy, Washington, D. C.; W. T. Engle, Grand Island, Neb.; Nathan Rosewater, Cleveland; H. E. Dunlop, Canton, Mo.; C. C. Conover, Kansas City, Mo.; J. W. Bolton, Iola, Kan.; L. Leroy, Memphis, Tenn.; J. D. Reid, Pilger, Neb.; W. H. Philp, St. Francis, Ark.; H. R. St. John, Alton, Kan.; G. R. Neff, Farmington, Iowa, and William F. Boos, Boston.

Dr. James B. Herrick, Chicago, read a paper on "Certain Popular but Erroneous Notions Concerning Angina Pectoris." Discussed by Drs. Joseph L. Miller, Chicago; G. W. McCaskey, Fort Wayne, Ind.; Gustav Baar, Portland, Ore.; S. P. Child, Kansas City, Mo.; J. A. Witherspoon, Nashville, Tenn.; Allen A. Jones, Buffalo, N. Y., and James B. Herrick, Chicago.

Drs. Thomas A. Claytor and Walter H. Merrill, Washington, presented a paper on "Orthodiagraphy: Presentation of a Series of Diagrams of the Heart and Aorta, with Explanatory Remarks."

Dr. James G. Van Zwaluwenburg, Ann Arbor, Mich., read a paper on "The Diagnostic Value of the Orthodiagram."

These two papers were discussed by Drs. Sidney Lange, Cincinnati; Thomas A. Claytor, Washington, and James G. Van Zwaluwenburg, Ann Arbor, Mich.

Thursday, June 9—Morning

The Committee on Nominations nominated the following: Chairman, Dr. A. Allen Jones, Buffalo, N. Y.; Vice-Chairman, Dr. D. C. L. Green, St. Paul, Minn.; Secretary, Dr. Wilder Tileston, New Haven, Conn.; Delegate, Dr. J. A. Capps, Chicago; Alternate, Dr. Alexander Lambert, New York; Orator, Dr. C. F. Hoover, Cleveland.

It was moved, seconded and carried that the Secretary be instructed to cast a ballot for these nominees.

Dr. Kate C. H. Mead, Middletown, Conn., read a paper on "Persistent Patency of the Ductus Arteriosus, Stenosis of the Isthmus of the Aorta, with Degeneration of the Coronaries of the Cardiac Muscle and of the Sino-Auricular Bundle." Discussed by Dr. Wilder Tileston, New Haven, Conn.

Dr. C. F. Hoover, Cleveland, read a paper on "Regional Vasomotor Hypertonus, with a Report of a Case." Discussed by Drs. Judson Daland, Philadelphia, and C. F. Hoover, Cleveland.

Drs. L. F. Barker, A. D. Hirschfelder and G. M. Bond, Baltimore, presented a paper on "The Electrocardiogram in Clinical Diagnosis." Discussed by Drs. M. J. Lichty, Cleveland; John H. Musser, Philadelphia, and A. D. Hirschfelder, Baltimore.

Dr. Claude A. Smith, Atlanta, Ga., read a paper on "Hookworm Infection and its Prevention." Discussed by Drs. Henry B. Ward, Urbana, Ill.; B. B. Bagby, West Point, Va.; C. C. Bass, New Orleans; Morgan Smith, Little Rock, Ark.; William Letterer, Nashville, Tenn.; John William Colbert, Albuquerque, N. M., and Claude A. Smith, Atlanta, Ga.

Drs. Louis B. Wilson and Byrd C. Willis, Rochester, Minn., read a paper on "Pathologic Relationship of Ulcer and Carcinoma of the Alimentary Canal." Discussed by Drs. H. E. Robertson, Minneapolis; J. N. Hall, Denver; Frank Wilbur Foxworthy, Indianapolis; D. C. Walt, Little Rock, Ark.; Charles G. Stockton, Buffalo, N. Y.; Richard Weil, New York; John A. Lichty, Pittsburg, Pa.; Abraham Jacobi, New York; Hugo A. Freund, Detroit; Harvey G. Beck, Baltimore; G. C. Smith, Boston; Frank Smithies, Ann Arbor, Mich.; T. Potter, Indianapolis, and Louis B. Wilson, Rochester, Minn.

THURSDAY, JUNE 9—AFTERNOON

Dr. H. D. Arnold, Boston, read a paper on "The Importance of a Low Protein Diet in Chronic Nephritis." Discussed by Drs. G. C. Smith, Boston; P. S. Roy, Washington, D. C., and H. D. Arnold, Boston.

Dr. W. W. Duke, Baltimore, read a paper on "The Relation of Blood Platelets to Bleeding in Certain Cases of Purpura." Discussed by Drs. J. H. Pratt, Boston, and W. W. Duke, Baltimore.

Dr. John D. Dunham, Columbus, Ohio, read a paper on "Clinical Results of Gastroenterostomy for Non-Malignant Diseases." Discussed by Drs. Judson Daland, Philadelphia; M. J. Lichty, Cleveland, Ohio; John A. Witherspoon, Nashville, Tenn.; DeLancey Rochester, Buffalo, N. Y.; A. L. Benedict, Buffalo, N. Y.; Gustav Baar, Portland, Ore., and John D. Dunham, Columbus, Ohio.

Dr. M. J. Lichty, Cleveland, read a paper on "The Influence of Perigastric Lesions on Gastric Secretions, Based on Clinical and Experimental Study." Discussed by Drs. DeLancey Rochester, Buffalo, N. Y.; James T. Pilcher, Rochester, Minn.; A. L. Benedict, Buffalo, N. Y.; G. C. Smith, Boston; Gustav Baar, Portland, Ore.; John A. Lichty, Pittsburg, Pa., and M. J. Lichty, Cleveland, Ohio.

Dr. Gustav Baar, Portland, Ore., read a paper on "Indicanuria." Discussed by Drs. DeLancey Rochester, Buffalo, N. Y.; Judson Daland, Philadelphia; Jay I. Durand, Atlantic City, N. J.; C. Shattinger, St. Louis, and Gustav Baar, Portland, Ore.

Drs. Judson Daland and George E. Pfahler, Philadelphia, presented a paper on "The Roentgen Ray in the Diagnosis of Diseases of the Alimentary Tract." Discussed by Drs. J. N. Hall, Denver; A. W. Crane, Kalamazoo, Mich.; M. J. Lichty, Cleveland, and Judson Daland, Philadelphia.

FRIDAY, JUNE 10—MORNING

Dr. Anders Frick, Chicago, read a paper on "The Different Forms of Mediastinal Exudative Pleurisy, with Report of Three Cases." Discussed by Drs. DeLancey Rochester, Buffalo, N. Y.; Frank Smithies, Ann Arbor, Mich., and Anders Frick, Chicago.

Dr. Frank Smithies, Ann Arbor, Mich., read a paper on "The Diagnostic Significance of the Paravertebral Triangle of Percussion Dulness (Grocco's Sign)." No discussion.

Dr. Edward C. Rosenow, Chicago, read a paper on "Autogenous Vaccine Therapy in Endocarditis." No discussion.

Dr. Willard J. Stone, Toledo, Ohio, read a paper on "The Treatment of Typhoid Carriers, with Report of a Case Treated by Inoculations of Typhoid Vaccine." Discussed by Drs. John J. Buettner, Syracuse, N. Y.; James J. Terrill, Galveston, Tex., and Willard J. Stone, Toledo, Ohio.

A STUDY OF MISTAKEN DIAGNOSES

BASED ON THE ANALYSIS OF 1,000 AUTOPSIES AND A COMPARISON WITH THE CLINICAL FINDINGS

RICHARD C. CABOT, M.D.

BOSTON

The subject of this paper was suggested by my experiences in a weekly conference with senior medical students at the Harvard Medical School. At this conference the organs obtained from all the autopsies performed at the Massachusetts General Hospital during the week preceding are brought before the class. Before the demonstration of each set of organs I discuss with the students a type-written summary of the clinical findings in the corresponding patient, including the history, the physical examinations, the reports on blood, urine, stomach contents and feces, the *x*-ray plates and all other data on which diagnosis was based during life. I never let anyone inform me beforehand of the autopsy findings. After we have committed ourselves definitely regarding the pathologic changes which we expect to find the hospital pathologist, Dr. Oscar Richardson, reads the autopsy protocol and demonstrates the organs.

In this exercise I have been forced once a week for three years to compare my diagnoses with post-mortem findings. It has proved so salutory and instructive, especially when I have been mistaken, that it has seemed to me well to summarize the results of a large series of comparisons between the judgments arrived at by a careful study of clinical data and the anatomic conditions revealed post mortem.

I. METHODS USED IN THE STUDY

I must first explain, as nearly as I can, the plan followed. It is not a simple matter to collate ante-mortem and post-mortem data in an intelligent way. One cannot simply read off the clinical diagnoses and note their correspondence or lack of correspondence with the anatomical findings, for:

1. It is often obvious when one reads the clinical record that the diagnosis has been copied from the autopsy protocol.

2. The clinical diagnosis may be so abbreviated as to omit important facts known during life. For example: When death occurs from heart disease the clinical diagnosis is often recorded merely as "mitral stenosis" without any statement regarding cardiac hypertrophy, dropsical effusions or terminal infections. Yet on reading the details of the record one may find evidence that the heart was enlarged, that a large amount of serous fluid has been removed from the abdomen and, perhaps, that some micro-organism had been isolated during life from the circulating blood. These facts warrant us in filling in the clinical diagnosis by the addition of a number of details. My comparisons, then, have been made between the diagnosis warranted by the recorded clinical data and the autopsy protocols.

3. In some cases it has been clear, after a little study, that the clinical diagnosis actually written on the records had been hurriedly filled in by an intern and did not represent the opinion of the attending physician. I recall one case in which the clinical diagnosis still stands as "neurasthenia" although the autopsy record shows that the patient died of cancerous pleurisy.

My comparisons, then, have been far from literal. In each case I have gone behind the recorded diagnoses and endeavored to reason out what diagnosis was jusified by the facts as known during life. No other course was open to me if I was to avoid some quite ludicrous mistakes.

II. TYPES OF ERROR

In the accompanying tables I have attempted (a) to separate correct diagnoses from mistaken ones and (b) to subdivide the mistakes into errors of omission and errors of commission. By an "error of omission" I mean failure to find some lesion which in all probability contributed to kill the patient; for example, the failure to find a pneumonic solidification.

"Burnt out" or obsolete lesions are often undiscovered during life and lead, therefore, to a discrepancy between ante-mortem and post-mortem findings, a discrepancy of interest but different from what I am now defining as an "error of omission." If, for example, the autopsy revealed pleural adhesions, and I am convinced from the written record and from my knowledge of the methods used in the hospital wards that these lesions did not contribute materially to the patient's last illness, and that no attempt was made to find these adhesions by testing the mobility of the lung borders or by any other method of investigation, I do not class the resulting discrepancy between anatomic and clinical results as an error of omission.

By an "error of commission" I mean the diagnosis during life of a lesion—such as cancer of the stomach—which autopsy shows is absent. This type of error is defined in contrast with some discrepancies regarding which we need not consider the autopsy as the court of last appeal. If, for example, a diagnosis of mitral regurgitation is recorded on the clinical record but not in the autopsy protocol, I consider this no proof that the clinical diagnosis is wrong. It is quite conceivable that the valve was insufficient during life owing to a muscular relaxation of which no convincing evidence is left after death. I have, therefore, attempted no comparison between the clinical and anatomic findings regarding mitral regurgitation. On the other hand, if mitral stenosis exists during life it should be demonstrable after death.

I shall now take up some of the statistics which represent our experience in the last thousand autopsies coming from the medical wards of the Massachusetts General Hospital.

III. DIAGNOSTIC ERRORS IN CERTAIN DISEASES OF THE HEART AND VESSELS

MITRAL STENOSIS

Correct diagnosis in	49 cases or 69 per cent.
Error of omission in	16 cases or 22 per cent.
Error of commission in	6 cases or 9 per cent.
Total,	71 cases

Most of these errors of omission were due to the fact that the patients were seen first within twenty-four hours of death, i. e., after the murmur had disappeared and at a time when very little evidence remained on which a diagnosis could be based.

Cases in which we mistakenly supposed that mitral stenosis existed are not so numerous as I had anticipated. Apparently we have learnt pretty well the lesson taught by Austin Flint nearly half a century ago. It seems to me well to emphasize here a fact often recorded, especially by English observers, but not sufficiently realized in this country. I refer to the presence of a presystolic murmur at the apex of the heart despite a sound mitral valve, not merely in cases of aortic regurgitation (as noted by Flint), but in any disease which has resulted in marked enlargement of the heart. In cases of chronic nephritis, pericardial adhesions, arteriosclerosis and hyperthyroidism, or any other cause, we often hear the murmur formerly identified with mitral stenosis. The murmur may be constant or transient. It may or may not be associated with a sharp, snapping first sound and an accentuated pulmonic second. It cannot be distinguished with any certainty from the murmur produced by mitral stenosis and will continue to lead us into error from time to time until

some other and more accurate methods of diagnosis are discovered.

I have found it best systematically to disregard all presystolic murmurs heard at the apex of a markedly enlarged heart, unless the case has been under observation long enough for us to have recorded the murmur before the heart became markedly enlarged or unless we have a clear history of a long-standing infectious process, presumably involving the heart valves. In renal cases, arteriosclerotic cases and, indeed, in most patients beyond their fiftieth year, presystolic murmurs are of very little significance.

AORTIC STENOSIS

Correct diagnosis in	19 cases or 61 per cent.
Error of omission in	11 cases or 36 per cent.
Error of commission in	1 case or 3 per cent.
Total,	31 cases

I have been surprised to note that the diagnosis of aortic stenosis (always accompanied in this series by a regurgitant lesion) was correctly made in nearly two-thirds of our cases, and especially was I amazed that in only one case did we commit ourselves wrongly to this diagnosis during life. It used to be a standing joke among our pathologists that the clinician always diagnosed aortic stenosis when only a roughening of the aortic arch was demonstrable post mortem. On the other hand, I have been equally astonished to learn that the pathologists found aortic stenosis so frequently where we had overlooked it during life. I am quite convinced that this lesion is often impossible of diagnosis by our present methods of physical examination. In this connection the following points have recently been impressed on me:

1. Aortic stenosis may exist despite the presence of an accentuated aortic second sound, although, as a rule, this sound is diminished or absent.

2. Aortic stenosis may exist in association with a "water-hammer" or "Corrigan" pulse, though the rule is against this. How these two facts are to be accounted for I have no idea.

3. With long-standing cases of "rheumatic" endocarditis involving the aortic valve in patients under 35 years of age, aortic stenosis is almost always present (as proved post mortem) whether there are any characteristic physical signs pointing to it or not.

AORTIC REGURGITATION

Correct diagnosis in	57 cases or 84 per cent.
Error of omission in	5 cases or 7 per cent.
Error of commission in	6 cases or 9 per cent.
Total,	68 cases

It will be noted that in the present series, as in that previously mentioned in my "Physical Diagnosis," our largest percentage of correct diagnoses in diseases of the cardiovascular system concern aortic regurgitation. This percentage was possible only because we have made it a rule to disregard diastolic murmurs unless there were vascular phenomena to correspond ("water-hammer" pulse, capillary pulse, etc.). Diastolic murmurs without these vascular phenomena have generally turned out, post mortem, to be associated with a sound aortic valve. I appreciate that the figures here presented regarding aortic regurgitation have less value than those relating to the stenoses, since it is impossible to deny that the aortic ring might stretch during life sufficiently to produce regurgitation and yet show no evidence of such stretching post mortem. Yet, for reasons which I cannot here take the space to present, I do not believe that the error attributable to this possibility is a considerable one.

CHRONIC MYOCARDITIS

Correct diagnosis in	13 cases or 22 per cent.
Error of omission in	15 cases or 26 per cent.
Error of commission in	31 cases or 52 per cent.
Total,	59 cases

I have given up making the diagnosis of chronic myocarditis, and I believe that the term should be stricken from our text-books on the practice of medicine. It is an anatomic condition, like acute interstitial nephritis, having no corresponding manifestations recognizable during life. A correct diagnosis of chronic interstitial myocarditis, of acute degeneration of the myocardium such as occurs in fevers, or of the fatty change observable in most cases of pernicious anemia, is wholly a matter of luck. There are no clinical symptoms and no physical signs constantly associated with any one of these conditions.

When a patient has suffered from well-marked angina pectoris and shows clear evidence of arteriosclerosis in the brain, the kidney or the peripheral arteries, we may guess that his coronary arteries are somewhat narrowed and that a fibrous myocarditis has resulted. But even then we may be wrong, as I have often been convinced post mortem. The evidence on which the diagnosis of myocarditis is ordinarily based points merely to a *myocardial insufficiency* such as may be produced by a great variety of causes without the presence of any granular, fatty or fibroid change in the heart. Further, the anatomic diagnosis of fibrous myocarditis post mortem is satisfactory only when it is positive. To say that a fibrous myocarditis does not exist one must have cut the heart into mince-meat and then sectioned and stained each morsel of the hash. The absence of gross fibroid changes demonstrable after a few knife-cuts into the ventricular walls, by no means excludes an extensive though microscopic fibroid change.

One of the most surprising things in this series of autopsies has been the not infrequent occurrence of gross fibroid myocarditis in hearts which were perfectly sufficient during life, and the still more frequent absence of any demonstrable lesion post mortem in hearts that were markedly insufficient during life. As will be seen

by the figures quoted above we were wrong in more than four cases out of five in our diagnosis of myocarditis.

ARTERIOSCLEROSIS

Correct diagnosis in	131 cases or 60 per cent.
Error of omission in	77 cases or 35 per cent.
Error of commission in	12 cases or 5 per cent.
Total,	220 cases

Most of the correct diagnoses in this group rested on inferences from general knowledge of pathology rather than on physical examination. If a patient has symptoms pointing to a non-traumatic cerebral hemorrhage it is fairly safe to assert that cerebral arteriosclerosis will be found, especially if the sufferer is middle-aged or older. If angina pectoris has tortured a man for months, it is very probable that his coronary arteries are diseased.

THORACIC ANEURISM

Correct diagnosis in	12 cases or 50 per cent.
Error of omission in	10 cases or 42 per cent.
Error of commission in	2 cases or 8 per cent.
Total,	24 cases

In two cases a mistaken diagnosis of aneurism was made owing to too great reliance on x-ray findings, in the absence of other important evidence. In one case I believe that the mistake cost the patient his life. Supposing his malady to be incurable, we allowed him to use narcotics for pain to an extent that ultimately proved fatal. At autopsy there was no trace of aneurism or of any other sufficient cause for death.

The classical difficulty of deciding between thoracic aneurism and mediastinal tumor has occurred five times in this series; in every case the autopsy showed aneurism. As a result of these and other experiences in this field I have come to use the following rule: When still in doubt between aneurism and tumor after all proper methods of investigation have been exhausted call it aneurism.

Abdominal aneurism is distinctly rare in my field of work, occurring but three times in 2,000 autopsies. Our autopsy material includes a relatively small number of syphilitics. Possibly it is for this reason that I have been taught by experience that when we have our annual or semi-annual discussion about the bed of a hospital patient who complains of epigastric pulsation ("aneurism or dynamic aorta?") the doubtful cases always turn out not to be aneurism, i. e., the patients recover and remain well when reassured.

CARDIAC HYPERTROPHY AND DILATATION

Correct diagnosis in	223 cases or 66 per cent.
Error of omission in	113 cases or 33 per cent.
Error of commission in	3 cases or 1 per cent.
Total,	339 cases

Had we relied wholly on palpation, percussion and auscultation for the estimation of the heart's dimensions I feel sure that our failures would have been far more numerous. Blood-pressure estimations have helped us greatly, and if we could have employed fluoroscopy in every case we could doubtless have done far better.

The distinction between dilatation and hypertrophy has not been successfully made in this series. What clinically seemed an acute dilatation has usually turned out after death to be a chronic hypertrophy and dilatation.

It will be noticed that in six of the seven types of cardiovascular disease thus far discussed, the percentage of failures ranges in the neighborhood of 33 per cent.; thus:

Aneurism	48 per cent.
Arteriosclerosis	40 per cent.
Aortic stenosis	39 per cent.
Hypertrophy and dilatation	34 per cent.
Mitral stenosis	31 per cent.
Aortic regurgitation	16 per cent.
Average	34 per cent.

In the acute infectious lesions presently to be discussed our record is so different as to indicate that from the diagnostic standpoint they belong in a different and less accessible class. But before passing to the consideration of these more difficult diagnostic problems I wish to return for a moment to some of the difficulties attending the diagnosis of mitral regurgitation. I have not attempted to estimate the number or the nature of our failures in the diagnosis of this lesion because we have, in my judgment, no standard by comparison with which we can get our bearings. But the study of hearts before and after death has further convinced me that mitral regurgitation (that commonest of all cardiac diagnoses) is not only an unverifiable but usually a superficial judgment—about as definite as tachycardia. What we chiefly need to know about mitral regurgitation is what is behind it. Does the orifice leak because of an infectious process involving the myocardium, because of a chronic nephritis which has thickened and stretched the heart, because of hyperthyroidism, beer or arteriosclerosis? Or, rarest of all, is there a purely mechanical deformity of the valve or valve curtains? In all cases, except those belonging to this last group, i. e., in at least nine-tenths of all cases in which we are likely to make the diagnosis of mitral regurgitation we should add it, like an appendage, to some other and more fundamental designation. Thus, such diagnoses as "chronic nephritis, hypertension, cardiac hypertrophy and dilatation with mitral regurgitation," or "arteriosclerosis, myocardial insufficiency, relative mitral incompetence," or "infectious arthritis and myocarditis with mitral leakage," should, I think, replace the great majority of those now standing on our record-books simply as "mitral regurgitation."

The origin, prognosis, course, probable complications and treatment—all that is most important about the case—is suggested not by the leakage but by the diseases which have produced it and are indicated in the earlier parts of the diagnoses above suggested. As I look over

the annual reports of our hospitals and note the great number of cases recorded merely as mitral regurgitation, it seems to me hardly more sensible than if one made so many diagnoses of "short breath" or "cough."

ACUTE ENDOCARDITIS AND ULCERATIVE ENDOCARDITIS

Correct diagnosis in	23 cases or 39 per cent.
Error of omission in	32 cases or 54 per cent.
Error of commission in	4 cases or 7 per cent.
Total,	59 cases

ACUTE PERICARDITIS

Correct diagnosis in	11 cases or 20 per cent.
Error of omission in	38 cases or 70 per cent.
Error of commission in	5 cases or 10 per cent.
Total,	54 cases

Most of the errors listed in these two groups are, I believe, inevitable at the present time. There are usually no distinctive physical signs either of acute endocarditis or of acute pericarditis, especially when they occur in the terminal stages of chronic disease. Fortunately it makes at present very little difference in our treatment whether we recognize these items of a general infection or not.

IV. RESPIRATORY SYSTEM

LOBAR PNEUMONIA

Correct diagnosis in	116 cases or 74 per cent.
Error of omission in	23 cases or 15 per cent.
Error of commission in	18 cases or 11 per cent.
Total,	157 cases

Regarding these cases of lobar pneumonia two comments seem to me worth making. First, it should be explained that some of the successful diagnoses of lobar pneumonia were made without distinctive physical signs of a process of reasoning which issued in the judgment "That is the sort of case in which a terminal pneumonia might well occur." This sort of reasoning works backward from familiar disease-groups previously

encountered post mortem. One recognizes during life one or more members of such a group and infers the presence of another. Alcoholism and trauma with an unexplained fever and leukocytosis is a familiar group pointing in the majority of cases to a larval pneumonia not revealed by the pulmonary signs. Such an inference is very far from being inevitable, yet experience has convinced many that reasoning of this type is valuable if used cautiously and provided it always goes hand in hand with a thorough study of the patient's history and of the present condition.

Another observation is suggested by the numerous diagnoses of pneumonia when this condition was not actually present. Such mistakes were especially common in patients who were comatose or partially so. The type of congestion or "settling" often found post mortem in the lungs of such sufferers may produce all the classic signs of a full-blown lobar pneumonia though absolutely no solidification; nothing but a soggy lung is discoverable after death. I have often had a similar experience in cases involving marked cardiac insufficiency with or without a considerable degree of hydropericardium. The signs apparently of solidification at the left base (in the so-called "pressure area" of pericardial effusion) associated with fever, leukocytosis and cough have often led me to a false diagnosis of pneumonia no sign of which was discernible post mortem.

BRONCHOPNEUMONIA

Correct diagnosis in	31 cases or 33 per cent.
Error of omission in	60 cases or 64 per cent.
Error of commission in	3 cases or 3 per cent.
Total,	94 cases

One might imagine that the very large percentage of error in our diagnoses of bronchopneumonia arose from the inclusion of infants and young children whose lungs are notoriously apt to show after death (from whatever cause) unsuspected areas of bronchopneu-

monia. But this table contains only cases of adults. I excluded all the cases of younger patients because I felt from the start quite hopeless of successful prediction in this field.

I feel convinced, however, that we may apply to adults the old adage of the pediatric specialists: "When you have the signs of bronchitis but the patient is obviously too sick for (simple) bronchitis, call it bronchopneumonia."

I have been much impressed by a series of typhoid patients dying with the signs only of bronchitis but showing extensive bronchopneumonic areas post mortem, and I am inclined to believe that in many "bad colds" the patch of "sticky râles" which hangs on for a week or more in one or another lower lobe posteriorly represents in fact a bronchopneumonia.

PHTHISIS (ACTIVE)

Correct diagnosis in	32 cases or 59 per cent.
Error of omission in	16 cases or 30 per cent.
Error of commission in	6 cases or 11 per cent.
Total,	54 cases

MILIARY TUBERCULOSIS

Correct diagnosis in	28 cases or 52 per cent.
Error of omission in	20 cases or 37 per cent.
Error of commission in	6 cases or 11 per cent.
Total,	54 cases

In explanation of these tables we must note that:

1. I have left wholly out of the account the numerous cases of obsolete or healed phthisis.

2. The 30 per cent. of unrecognized cases was made up mainly of cases seen for the first time within a few hours of death, when all distinctions are blurred.

3. In the effort to recognize doubtful incipient cases we have frequently used radiography, but so far without getting any reliable information not obtainable by other methods. An increased resistance to the passage of x-rays is an excessively delicate but also a very gen-

eral indication, capable of a multitude of explanations and produced by a multitude of causes other than tuberculosis and often indistinguishable from each other by radiographic evidence.

The correct diagnoses of miliary tuberculosis would have been much fewer had we not adopted some years ago the rule, "When a case is clinically one of tuberculous meningitis, call it miliary tuberculosis and you will rarely be contradicted at autopsy." Tuberculosis is practically never confined to the meninges, though in many cases miliary processes make themselves apparent only in the central nervous system.

V. URINARY SYSTEM

ACUTE NEPHRITIS

Correct diagnosis in	5 cases or 16 per cent.
Error of omission in	20 cases or 62 per cent.
Error of commission in	7 cases or 22 per cent.
Total,	32 cases

Some years ago I undertook a critical study of the urinary reports and post-mortem findings in the different types of nephritis. I was much impressed at that time with the large percentage of mistaken diagnoses of acute nephritis—especially the errors of omission. In the present study of another series of cases, the same facts claim attention. It must be stated at the outset that our material contains no cases of scarlet fever; very few of diphtheria and that, as we have no maternity department, our cases of the puerperal type are confined mainly to eclampsia. In the material so limited we find almost no recognizable cases of acute nephritis. Most of those which in former years we called acute we now recognize (thanks to blood-pressure measurements) as chronic with acute exacerbations. For prognosis, and in a lesser degree for treatment, this distinction is important.

Our cases of acute nephritis, recognized and unrecognized, belong mostly in one of three groups:

1. Those due to pneumococcus infections.
2. Those due to infection by the organism of septic endocarditis.
3. Those due to mercurial poisoning.

Our verified diagnoses of acute nephritis have been made chiefly by following these etiologic hints and not from the urinary findings. Given a case of mercurial poisoning, of general pneumococcus infection or of "malignant endocarditis," with or without arthritis, and it is fairly safe to predict that an acute nephritis will develop and will be demonstrated post mortem if the issue is fatal. But this is not a secure basis for diagnostic structures, and we have not yet been able to build much on this or on any other foundation. We doubt whether others can do better at the present time.

CHRONIC GLOMERULAR NEPHRITIS

Correct diagnosis in	53 cases or 74 per cent.
Error of omission in	9 cases or 12 per cent.
Error of commission in	10 cases or 14 per cent.
Total,	72 cases

CHRONIC INTERSTITIAL NEPHRITIS

Correct diagnosis in	25 cases or 50 per cent.
Error of omission in	19 cases or 38 per cent.
Error of commission in	6 cases or 12 per cent.
Total,	50 cases

In marked contrast with our failures in acute nephritis is our large percentage of success in chronic glomerular nephritis[1]—the type often termed chronic diffuse, chronic parenchymatous nephritis or secondary contracted kidney (Senator). Most of our errors were in patients seen only in the moribund state and the same is true of the failures recorded in chronic interstitial nephritis.

In distinguishing these two types of nephritis (i. e., those due probably to the results of early infection and

1. Judging by the averages of this whole study I consider anything over 66 per cent. of verified diagnoses as a "high" percentage of success, though I admit that even our best is far from brilliant.

those due to arteriosclerosis, wear and tear and senility) I have noticed that most of those associated with any considerable degree of anemia usually turn out to be of the glomerular type. Anemia and uremia are, perhaps, due to the same metabolic poison, while in the interstitial cases we have less anemia and less uremia—the symptoms being chiefly those of circulatory failure.

AMYLOID NEPHRITIS

Correct diagnosis in	0 cases or 0 per cent.
Error of omission in	4 cases or 100 per cent.
Error of commission in	0 cases or 0 per cent.
Total,	4 cases

RENAL TUBERCULOSIS

Correct diagnosis in	1 case or 33⅓ per cent.
Error of omission in	2 cases or 66⅔ per cent.
Error of commission in	0 cases or 0 per cent.
Total,	3 cases

RENAL NEOPLASM

Correct diagnosis in	1 case or 16⅔ per cent.
Error of omission in	5 cases or 83⅓ per cent.
Error of commission in	0 cases or 0 per cent.
Total,	6 cases

The figures in these three groups are too small to justify any discussion. It may be stated, however, that four out of five renal neoplasms were microscopic and that most of our cases of renal tuberculosis are successfully diagnosed and the patients operated on so that these figures are misleading both in extent and in significance.

VI. NERVOUS SYSTEM

CEREBRAL HEMORRHAGE

Correct diagnosis in	34 cases or 67 per cent.
Error of omission in	4 cases or 7 per cent.
Error of commission in	13 cases or 26 per cent.
Total,	51 cases

CEREBRAL TUMOR

Correct diagnosis in	8 cases or 72 4/5 per cent.
Error of omission in	2 cases or 18 1/5 per cent.
Error of commission in	1 case or 9 per cent.
Total,	11 cases

"Cerebral hemorrhage" is here used in the broad sense of "apoplexy," including all sudden attacks of coma and paralysis due to thrombosis, to acute softening or to embolism of the cerebral arteries. It is confessedly impossible to distinguish hemorrhage, rapid thrombosis and embolism by any study of the resulting disturbances of function. With this understanding it may be said that our diagnostic campaigns in this field have obtained an average degree of success. I have been struck, however, with the very considerable proportion of cases which presented during life the ordinary features of apoplexy but showed after death only an arteriosclerotic degeneration of the cerebral arteries without hemorrhage, embolism, thrombosis or acute softening. These cases are like some of those on which Pal based his interesting theory of vascular crises[2] as an explanation of apoplectiform seizures without demonstrable gross lesions post mortem.

Of the small group of cerebral tumors here studied, I will merely say that although we usually were correct in predicting the presence or absence of tumor somewhere within the skull, the attempts at localizing the growth were failures in most cases.

SEPTIC MENINGITIS

Correct diagnosis in	23 cases or 64 per cent.
Error of omission in	8 cases or 22 per cent.
Error of commission in	5 cases or 14 per cent.
Total,	36 cases

TUBERCULOUS MENINGITIS

Correct diagnosis in	26 cases or 72 per cent.
Error of omission in	5 cases or 14 per cent.
Error of commission in	5 cases or 14 per cent.
Total,	36 cases

2. Pal: Gefässkrisen, Berlin, 1905.

Under the general title of "septic meningitis" I have included the epidemic meningococcus cases, together with those due to the pneumococcus and the pyogenic organisms, whether invading the meninges from the middle ear or elsewhere. I shall omit discussion both of this group and of the tuberculous cases following.

VII. DIGESTIVE SYSTEM

GASTRIC CANCER

Correct diagnosis in	30 cases or 72 per cent.
Error of omission in	7 cases or 17 per cent.
Error of commission in	5 cases or 11 per cent.
Total,	42 cases

PEPTIC ULCER (GASTRIC OR DUODENAL)

Correct diagnosis in	9 cases or 36 per cent.
Error of omission in	14 cases or 56 per cent.
Error of commission in	2 cases or 8 per cent.
Total,	25 cases

HEPATIC CIRRHOSIS

Correct diagnosis in	19 cases or 61 per cent.
Error of omission in	9 cases or 30 per cent.
Error of commission in	3 cases or 9 per cent.
Total,	31 cases

Our relatively successful dealing with the neoplasms in this table forms a sharp contrast with the shocking failures which were the rule when the diagnosis of peptic ulcer was attempted. Among the fourteen ulcers which we failed to recognize during life nine were gastric and five duodenal. In two cases (Autopsies 637 and 1077) the patient had cirrhosis of the liver (ante-mortem and post-mortem diagnosis) and the gastric hemorrhages were attributed to this. Two patients (Autopsies 2278 and 3441) entered the hospital with the history, symptoms and signs of meningitis, which was confirmed at autopsy. In one case the history distinctly suggested ulcer; in the other, a tuberculous case, there were no symptoms pointing to the gastro-intestinal tract. Seven

patients (Autopsies 526, 1161, 1829, 1861, 2024, 2135, 2388) entered the hospital acutely ill with disease outside the gastro-intestinal tract (lobar pneumonia, cancer of the uterus with extensive metastases, cardiovascular degeneration, uremia, congenital syphilis, apoplexy, diabetes). One of these patients, a diabetic boy of 17, had had for three months stomach symptoms quite compatible with gastric ulcer though not characteristic of it. I doubt whether any surgeon would have wished to operate on him in his toxemic and emaciated condition. The other six of the seven patients last referred to had no gastric signs or symptoms whatever.

There remains a group of three cases out of the fourteen in which a diagnosis should, perhaps, have been made. One of them (Autopsy 1586) was seen twice by Drs. Maurice H. Richardson and F. G. Balch, who could make no diagnosis and advised against exploration on account of uncompensated heart disease (autopsy showed insufficiency of the mitral, aortic and tricuspid valves). The second case (Autopsy 1604) had a typical ulcer history, but the abdominal symptoms were obscured or disregarded on account of what was taken to be an acute pneumothorax. Autopsy showed a "subphrenic hypopneumothorax" pushing the diaphragm up to the level of the third rib in front. In view of the frequent occurrence of this type of subphrenic abscess after perforation of a peptic ulcer I think this diagnosis should have been made. The third patient (Autopsy 1064), a woman of 68, would permit no examination, far less exploration of her abdomen.

In two men, each 35 years old (Autopsies 1238 and 1405) we made the diagnosis of peptic ulcer and were contradicted at the autopsy. One had had "dyspepsia" for four years and was seized the night before he entered the hospital with violent epigastric pain and tenderness not associated, however, with muscular spasm. At autopsy next day a cyst of the pancreas was found to have ruptured into the peritoneum with a resulting general

peritonitis. The other man came to the hospital for persistent vomiting of ten days' duration. Soon after entrance he vomited 10 ounces of pure blood. He had also marked cerebral symptoms attributed by a neurologic consultant to cerebral syphilis. At autopsy the stomach showed nothing abnormal. Death was due to chronic interstitial nephritis.

VIII. MISCELLANEOUS

TYPHOID FEVER

Correct diagnosis in	53 cases or 92 per cent.
Error of omission in	0 cases or 0 per cent.
Error of commission in	5 cases or 8 per cent.
Total,	58 cases

DIABETES MELLITUS

Correct diagnosis in	19 cases or 95 per cent.
Error of omission in	0 cases or 0 per cent.
Error of commission in	1 case or 5 per cent.
Total,	20 cases

In typhoid and diabetes the percentage of errors is notably smaller than in the previous groups. This is what one would expect from the sharply cut symptomatology and semeiology of these diseases. Had these cases included any prior to the discovery of the Widal test the proportion of mistakes in the typhoid group would no doubt have been much larger.

The error in the diagnosis of diabetes occurred in a case which was under observation only a few hours before the fatal termination. What seemed to be diabetic coma turned out to be apoplexy with symptomatic glycosuria. It was afterwards learned that the urine had been examined previous to his seizure and had contained no sugar. His previous history showed nothing pointing to diabetes. It must be noted, however, that post mortem examination is not capable of refuting a well fortified ante-mortem diagnosis of diabetes.

The five cases in which typhoid fever was erroneously supposed to exist are of considerable interest and war-

rant brief analysis. They confirm the assertion which I have elsewhere made[3] that typhoid fever is simulated (in New England) by only two other diseases, tuberculosis and general septicemia. In this series two of the five cases supposed to be typhoid turned out to be cases of miliary tuberculosis; the other cases were general septicemia.

CASE 1.—One of the tuberculous patients (No. 1,111), an Italian laborer of 28, had had three weeks continued fever, averaging 101 F., with epistaxis, enlarged spleen and a positive Widal. There were numerous scattered râles in both lungs, but the sputum was negative. Later there were hemorrhages from the bowel, also from the gums and under the skin.

CASE 2.—The other case of miliary tuberculosis (No. 1,759) had no Widal reaction, but there was continued fever without demonstrable local cause, associated with an enlarged spleen and a leukocyte count of 2,700.

CASE 3.—In one of the three septic cases (No. 2,103) the patient gave a history of an attack of erysipelas from which he was convalescent (after three weeks' illness) when he entered the hospital. He had a continued fever (102-105 F.) a low white count and a "very suggestive" but not positive Widal reaction. The spleen was not felt; no rose spots. A septic wound on the scalp originating in a furuncle was still unhealed. The delirium was so active that meningitis was suspected, but lumbar puncture liberated 35 c.c. of sterile, apparently normal fluid. Blood-cultures in bile were likewise negative. After four days of fever he developed stiffness of the neck and a Kernig reaction. Death occurred on the fifth day of observation, about the twenty-sixth of his illness. Diagnosis: Typhoid. Autopsy: Streptococcus septicemia. Doubtless it was the low white count and the "very suggestive Widal" which threw us off the track.

CASE 4.—A second patient (No. 1,031) entered the hospital with a femoral phlebitis said to have occurred in tenth week of a typhoid with relapse. This diagnosis was accepted in spite of the absence of a Widal reaction. Soon after entrance the patient developed phlebitis in the other leg as well as a leukocytosis of 10,600. There were many bedsores, and evidences of what was interpreted as a small effusion in the right pleural cavity. On the day of his death after a month's illness, there was sharp pain in the right axilla. Autopsy

3. Cabot: The Three Long Continued Fevers of New England, Boston Med. and Surg. Jour., 1908.

showed multiple abscesses of the liver, thrombosis of the inferior cava both femorals and the right renal vein. No evidence of typhoid. This diagnosis should, I think, have been suspected owing to the absence of the Widal after ten weeks' illness and the development of a double phlebitis, which is rare in typhoid.

CASE 5.—The last case was one of ulcerative endocarditis (No. 1,503) which gave no distinctive evidence of its presence at any time. The patient had for three weeks a continued fever averaging 101.8 F. with rose spots and enlarged spleen. The leukocytes varied between 7,000 and 12,400. The Widal reaction was suggestive but never positive. Physical examination was negative until within a few days of his death, when a slight systolic murmur appeared at the apex. Next day there was deafness, ptosis of the right eyelid, stiff neck and a double Kernig's sign. The visiting physician's diagnosis was "typhoid"; the intern's, "general tuberculosis." Autopsy showed: Polypous endocarditis of the mitral valve, various embolisms, hemorrhage into the pia arachnoid of the cerebral hemispheres and general septicemia due to an atypical diphtheric bacillus.

SYPHILIS

Cerebral syphilis is a diagnosis quite frequently made at the Massachusetts General Hospital, but so far as I know it has never been both made and confirmed during the years (1899 to 1909, inclusive) covered by this report. Two cases with all the traditional evidences of cerebral syphilis, one of which had a positive Wassermann reaction, turned out to be tuberculous meningitis at autopsy; another case showed only chronic interstitial nephritis; in a fourth case multiple thromboses had occurred in the great venous sinuses of the cranium without any of the recognized causes for such thrombosis. In the only case actually characterized by intracranial syphilitic lesions post mortem they were not recognized in life.

Two other cases of syphilis have recently taught me lessons. One had the ordinary evidences of Banti's disease, splenomegaly and marked anemia followed some months later by ascites. The history gave no hint of syphilitic infection. Dr. Wilder Tileston found a per-

foration of the nasal septum and suggestive irregularities in the surface of the scalp and of the shin bones, just in time to save the patient from splenectomy. Under potassium iodid and mercury the ascites and anemia disappeared, the spleen shrunk to one-half its former size and the patient made a complete and lasting symtomatic recovery.

The other patient, said to have malaria, had chills, intermittent fever, enlarged spleen and malarial organisms in the blood. I found the liver also enlarged, no malarial organisms in the blood, and obtained a full history of previous syphilitic infection. All symptoms promptly disappeared a year ago under antisyphilitic treatment and have not recurred since.

In order to keep this paper from extending beyond its already inordinate length, I shall try to condense the rest of my data into maxims which should have the merit of brevity if not of wit or clearness, incorporating my summary and conclusions with them.

SUMMARY AND CONCLUSIONS

1. Never make a diagnosis of uremia in a patient seen for the first time in an acute illness characterized by coma or convulsions. Such diagnoses rarely turn out right.

2. Never make a diagnosis of ptomain poisoning without definite chemical evidence. General peritonitis or a tabetic crisis is usually the correct diagnosis.

3. Make no diagnosis of hysteria, neurasthenia or psychoneurosis in a patient whose symptoms begin after the forty-fifth year. The actual diagnosis is likely to be arteriosclerosis, hyperthyroidism, dementia paralytica, or pernicious anemia.

4. Diagnoses of tertian malaria in patients whose symptoms resist quinin more than three days are almost invariably wrong.

5. Bronchial asthma beginning after 40 usually spells heart or kidney disease.

6. Epilepsy beginning after 40 usually means dementia paralytica or cerebral arteriosclerosis.

7. Typical migraine is often a symptom of unrecognized brain tumor or chronic nephritis.

8. Most cases of "bronchitis" mean tuberculosis, bronchopneumonia or multiple bronchiectasis cavities.

9. Aside from the immediate results of acute infections (such as scarlet fever, diphtheria, tonsilitis and pneumonia) "acute" nephritis usually turns out to be chronic.

10. Acute gastritis and gastralgia usually mean appendicitis, gall-stones or peptic ulcer.

11. Pus in or near the liver is often mistaken for serous or purulent pleurisy, for it produces identical signs in the right chest posteriorly.

12. An *x*-ray of the shin-bones may give the first hint of an active syphilitic process in the joints or internal viscera.

13. Systolic or presystolic murmurs, heard best at the apex of a markedly enlarged heart, rarely mean valve lesions.

14. Diastolic murmurs at the base of the heart are very uncertain evidence of aortic disease unless there are characteristic jerkings in the peripheral arteries.

15. Myocarditis is a diagnosis which should never be made clinically.

16. Besides the direct evidence afforded by the history and the various methods of physical and chemical examination, diagnosis profits much by taking account of certain familiar pathologic chains or groups of them. Given one or two members of the group it is often wise to act as if the other were present, provided, of course, that the direct evidence in no way contradicts us.

17. Cerebral localization applied to tumors, hemorrhages and the like is still in its infancy.

18. The clinical diagnosis of the so-called diseases of the blood is the easiest and safest in medicine.

190 Marlboro Street.

EXPERIENCES WITH THE DUODENAL CONTENTS

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The examinations of stomach contents, which were inaugurated forty years ago by Kussmaul and later by Ewald, Leube, Boas, Riegel and others, have now been generally introduced into the clinical investigation of digestive disturbances.

The rôle which the stomach and its secretion play in the digestive process has formerly been estimated a great deal higher than at present. At first it was determined that human beings could exist very comfortably without any gastric juice at all (as proved by the numerous cases of achylia gastrica); then it was proven by the surgeons (Schlatter) that the stomach could be excised *in toto* without fatal consequences.

By physiologists as well as by clinicians the principal work of the stomach is now considered to be rather a preparatory process for the real digestion in the small intestine. The principal juices for the latter are contained in the duodenum. The potent pancreatic juice, the bile and the duodenal secretion are here poured out. The mixed juices have to fulfill two purposes, first, to make all nutritive materials ready for absorption and second to neutralize the strongly acid gastric contents; for the intestinal wall cannot, as a rule, stand free acids for any length of time.

It is, therefore, self-evident that any information as to the condition of the duodenal secretions would be of

vast importance. Until recently this was considered hardly possible. Since I introduced the duodenal pump.[1] however, the duodenal contents can readily be obtained, and I have therefore, made some investigations on its properties in a number of cases.

The method consisted generally in having patient drink in the fasting condition tea with sugar, without milk and then about half to three-quarters of an hour later introducing the duodenal pump, the patient meanwhile drinking a half tumblerful of water. Later, after one-half to one hour, the patient drinks a glassful of seltzer or hot water or tea and the examination then takes place. Whereas formerly I obtained the duodenal contents through continuous aspiration I now proceed differently, making suction first by means of a syringe and as soon as the contents are obtained removing the piston of the syringe and keeping the barrel of the syringe low. The fluid is thus siphoned out in a slow stream.

I have laid down the results of these examinations in the accompanying table.

COMMENT ON TABLE

If we analyze all the cases of the table we first meet six cases of nervous dyspepsia (1-6) in which trypsin was absent once in the duodenal juice.

In case 8 (chronic gastritis and nervous vomiting) the duodenal contents were thick and turbid, which might point to a duodenal catarrh. In Case 11 (T), with atony of the stomach, steapsin was absent in three examinations and once in examining the duodenal contents in the fasting and dry state (11 E.) all the ferments were found to be absent. In the same patient (11 F.) thick mucus was found once in the duodenal contents after an attack of ptomain poisoning. I append the *x*-ray pictures taken of this patient with the duodenal pump *in situ* (Fig. 1-2).

1. Einhorn, Max: A Practical Method of Obtaining the Duodenal Contents in Man, Med. Rec., Jan. 15, 1910.

In Case 14 (severe hyperchlorhydria and atonic dilatation of the stomach), in Case 17 (ulcer of the stomach with continuous vomiting), and in Case 33 (hypertrophic cirrhosis of the liver with chronic jaundice and intense hyperchlorhydria) the duodenal contents were acid and contained small quantities of free hydrochloric acid. The tests for the ferments were negative. In all other cases the contents were slightly alkaline or neutral and only rarely slightly acid. Case 15 (hyperchlorhydria and chronic enteritis) yielded a thick mucous fluid, to which later a pure golden yellow bile was added.

Seven cases of achylia of the stomach (19-25) showed twice an entire absence of trypsin and once a weak trypsin reaction whereas the other ferments were present. In one case of diabetes mellitus with normal stomach secretion (27) the contents showed absence of amylopsin, whereas the other ferments were present. Another case of diabetes with achylia (28) showed the presence of all the pancreatic ferments. In Case 29 (cholelithiasis and achylia gastrica) the contents were yellowish and turbid, but contained all the ferments. Four cases of chronic jaundice (30-33) showed the following result: in two (30 and 31) the duodenal contents did not reveal a trace of bile, while all the pancreatic ferments were present. In Case 32 a little bile was present once, another time it was absent. In Case 33 bile was present, mixed with mucus; hydrochloric acid was also present in small quantities.

Two cases of cirrhosis of the liver (without icterus) (34-35) showed good duodenal contents with bile; in one (34) trypsin digestion was very weak. In one case of cholecystitis (36) the contents were yellow but thick and turbid and showed no trypsin reaction.

Case 37 (cancer of liver) furnished a golden yellow juice mixed with mucus, showing all the pancreatic ferments. Case 38 (Banti's disease) showed normal duodenal contents. Case 39 (hyperchlorhydria and neuras-

thenia) showed weakened trypsin digestion and 40 (ulcer of stomach) normal duodenal contents.

In the column "Remarks" (Cases 7a, 11c and d, 35a, 37) a few experiments have been recorded, to test the relation of duodenal contents in reference to nucleus and connective tissue digestion (thymus and catgut). For comparison the effect of gastric contents on the same substances was noted in each instance. It was found that catgut as well as connective tissue (as contained in the raw thymus gland) can disappear entirely in neutral or weakly alkaline duodenal contents and that the nuclei of the thymus gland can also be digested in the stomach contents. Thus both these specific reactions (connective tissue for gastric digestion, and nuclei for pancreatic digestion) prove themselves to be entirely unreliable and without significance.

Among "remarks" we also find an experiment with secretin, showing the marked influence it has on the augmentation of secretion of bile and pancreatic juice (Case 11f).

I wish to emphasize particularly a few points.

1. Achylia Gastrica.—Among the seven cases of achylia gastrica trypsin was absent twice and once was only very weak, whereas steapsin and amylopsin were present. The disturbance of the pancreatic function in the above affection of the stomach explains why we frequently find intestinal troubles associated with it.

2. Admixture of Mucus.—An admixture of mucus with the duodenal contents occurs in two ways and is probably of some significance. The mucus may be evenly and intimately mixed with the contents, or it may appear at intervals in the relatively clear contents of the duodenum. The latter would point to the origin of the mucus from the duodenum, whereas its intimate admixture would point to its origin either in the pancreas or the bile passages. Presence of mucus in conjunction with other clinical symptoms (diarrhea, distress some

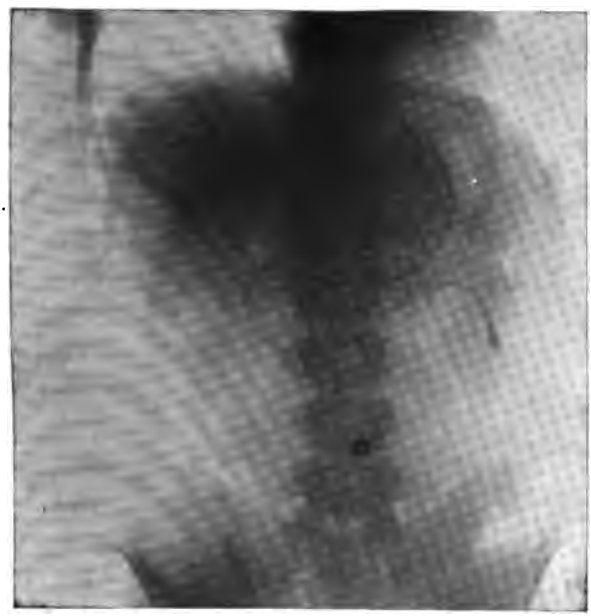

Fig. 1.—Patient T., with the duodenal pump in the small intestine previous to the ingestion of bismuth.

Fig. 2.—Patient T., with the duodenal pump in the small intestine, after the ingestion of bismuth. The contours of the stomach are visible. The tube of the duodenal pump is seen outside of the stomach in the duodenum and small intestine.

time after meals) would lead us to think of duodenal catarrh (Case 15, Mrs. H. H. R.).

3. Absence of Bile.—Occasionally we obtain on aspiration of the duodenal contents at first only a clear or slightly amber-colored fluid. It is of alkaline reaction and contains the pancreatic ferments. Usually after waiting a short time and after repeated aspirations a golden yellow fluid (containing bile) appears. This has no diagnostic significance. If, however, after patient waiting and aspirating, only pancreatic juice but no trace of bile appears, it may be of some importance, particularly in cases of chronic jaundice. If bile is present in the duodenal contents a complete occlusion of the common bile-duct can be excluded. If the bile is entirely missing and pancreatic juice is present, it points to the seat of the obstruction above the common duct.

Even if the results of these examinations are only meager, I should like to call attention to the fact that this field is entirely new and as yet hardly invaded. It might be expected that further work in the same direction will reap rich fruits not only with regard to diagnosis but also for therapy.

20 East Sixty-third Street.

A POSSIBLE DIFFERENTIAL SIGN BETWEEN CARDIAC DILATATION AND PERICARDITIS WITH EFFUSION

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In attempting to develop a differential sign I wish to acknowledge the dangers of generalizing from my limited material and of interpreting post-mortem findings as clinical signs.

While studying the details of the mechanics of the support of the normal and pathologic heart, some relations between the heart, right lung and liver turned my attention to the changes in the position of the liver due to dilatation of the right heart and to pericarditis with effusion. On analysis these changes seemed to be due to certain physical forces producing strains on given anatomic structures. As the nature and direction of these stresses are constant, varying only in degree, their effect should also be constant, varying only in degree. In the two lesions the physical forces present differ in that the support rendered the liver by the inferior cava through its connection with the heart and the connective tissue structures extending from the heart to the neck, is applied farther to the right in dilatation than in pericarditis. This difference in support of the liver may, when pressure is applied from above, cause a displacement of the liver to a degree possibly sufficient for a differential sign. The differential sign in cardiac dilatation is a high liver with a narrowed area of lung-liver relative dulness, and in pericardial effusion, a low liver

with a narrowed area of lung-liver relative dulness. This possible differential sign pertains only to large cardiac dilatation involving the right heart, from which a differential diagnosis of pericarditis with effusion is often most uncertain.

Full details leading to the essential physical and anatomic reasons for this difference in the position of the liver are too numerous to be given in a paper of this nature. Consequently the main facts will be stated, leaving details for future publications.

The material was fixed in formaldehyd solution, sectioned, measured, and each organ projected in a front and side view. In this way the position of each organ and its relation to neighboring organs can be quite accurately studied. The strain on certain parts of organs can also be determined by considering the direction of parts in the light of the forces at work.

Examples of extreme development of given conditions often call attention to principles which might otherwise be overlooked. Consequently two case will be described: first, a case of extreme dilatation of the right heart due to mitral stenosis; second, a case of extreme collapse of the heart due to pericarditis with effusion.

DESCRIPTION OF CASES

Points of Interest in Case 1

Sterum and ribs markedly depressed.

Heart as a whole displaced slightly into left thorax.

Valvular openings actually lower than normal but when located in terms of ribs they are only slightly displaced, especially when the size of the heart is considered.

Left ventricle about normal size.

Left auricle greatly dilated. Greater portion of right wall in front of the root of right lung.

Right ventricle greatly dilated. Has pushed left lobe of liver downward.

Right auricle greatly dilated.

That portion of inferior cava above diaphragm dilated to form part of the right auricle.

Auriculoventricular wall runs in almost a straight line from diaphragm to root of left lung; this includes a portion of the wall of the left auricle.

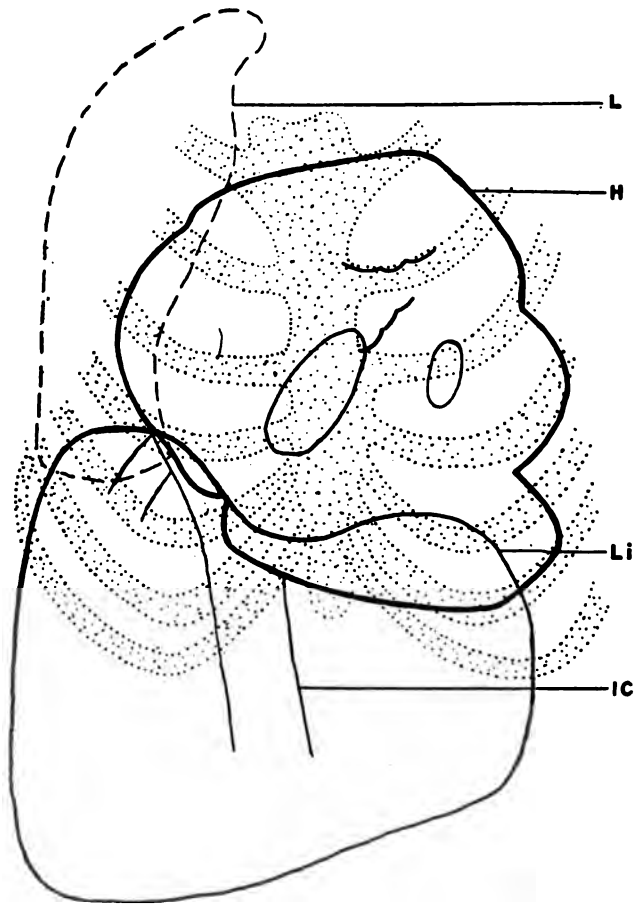

Fig. 1.—Mitral stenosis (Case 1) dilatation of left auricle, right ventricle, and auricle; position of heart (H) above reaching first rib, below, tip of ensiform cartilage, to left 9.5 cm., to right 8 cm.; right lung (L) 6.5 cm. to right of midsternal line, lower border in front in fourth interspace; liver (Li) enlarged, right lobe high, at fourth rib, hepatic veins open into right auricle at highest portion of right lobe, left lobe depressed; inferior cava, (IC) displaced to right with convexity to right.

Hepatic veins run in almost a perpendicular direction and open at the highest portion of the cupola of the right diaphragm into the right auricle.

Inferior cava dilated, displaced to right with convexity to right.

Liver (enlarged) has been pushed to right by the dilating right auricle and inferior cava. The right lobe has been held by the walls of the right auricle and inferior cava. This is shown by direction of walls and the course of the hepatic veins. Right lobe much higher than left—cupolated effect. Right lung pushed by left and right auricle upward, outward and backward.

Points of Interest in Case 2

Sternum and ribs only slightly depressed.

Heart swings near median line.

Valvular openings only slightly displaced.

All heart chambers collapsed.

Inferior cava above diaphragm stretched and that portion within the pericardium collapsed; near median line; congested but not greatly dilated.

Auriculoventricular wall almost a straight line.

Liver displaced downward; right lobe not held up as in Case 1; right and left lobe in almost the same plane.

Right lung pushed outward and backward by the pericardial sac; pleural adhesions prevent easy displacement of lung; these adhesions show signs of downward drag.

COMMENT

These findings lead one to believe that the attachment of the pulmonary veins to the connective tissues and other structures about the root of the lungs and the auriculoventricular wall attached to the large vessels and through the left auricle to the root of the lungs play an important rôle in the support of the heart. When the right heart is markedly dilated the auriculoventricular wall runs in almost a straight line from the diaphragm to the root of the left lung, thus indicating the support of hydraulic pressure and stress transmitted from diaphragm to the root of the left lung. The right wall of the right auricle and to some extent the right wall of the pericardium transmit to the root of the right lung a portion of the stress from the diaphragm. Fibrosis incidental to cardiac lesions increases the strength of the auriculoventricular wall.

As the heart dilates the central tendon of the diaphragm is lowered; the weight of the liver and the resistance offered the dilating heart are referred to the

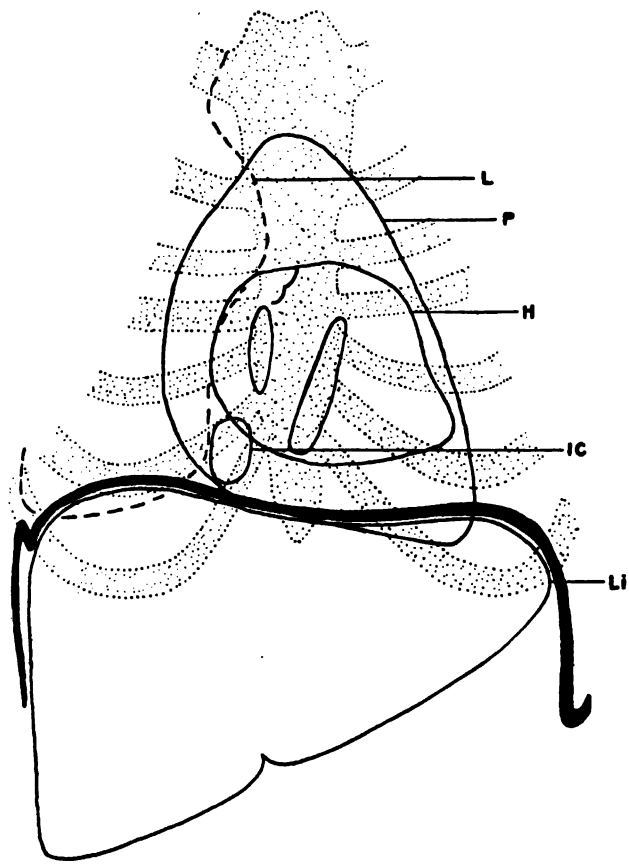

Fig. 2.—Pericarditis with effusion (Case 2); pericardial sac, P (dilatation not shown); heart, H (collapse cannot be shown; right lung (L) slightly displaced to right; pleural adhesions which have been pulled downward by pericardial pressure; liver (Li) displaced downward, upper surface of right and left lobes in almost same plane; inferior cava, (IC) not shown, but runs in almost a straight line.

walls of the right auricle and the auriculoventricular wall, thence to the root of the lungs and to the neck. Doubtless the column of blood materially supports the

vascular and cardiac walls. The support thus rendered the liver is applied in Case 1 at the openings of the hepatic veins in the inferior cava. The support thus given the liver prevents the actual depression of the right lobe to the same degree as that of the left. Consequently the right lobe is pulled up, producing the high cupolated effect. As the inferior cava dilates, the openings of the hepatic veins are pushed to the right and finally occupy the highest portion of the liver, which in Case 1 is the cupola of the right diaphragm.

Movements due to the dilatation of the heart, including the right heart in Case 1, are:

1. Descent of the sternum and ribs.
2. Descent of the heart and liver.
3. Apparent elevation of the right lobe of liver.
4. Displacement of the inferior cava to the right with convexity to the right.

In the fetus the following relationships are found:

1. Sternum high, ribs horizontal.
2. Right heart small.
3. Liver bilobed, two lobes of equal height.
4. Inferior cava near the median line with convexity to the left.

As development of the fetus to maturity advances the following changes are noted:

1. Descent of sternum, ribs in oblique position. The acquired descent of the ribs doubtless accounts in part for the apparent higher position (in terms of ribs) of the liver in adults as compared to the foetal position.
2. Descent of heart and liver.
3. Right heart enlarges.
4. Left lobe of liver atrophies and occupies a lower position, right lobe occupies a higher position.
5. Inferior cava moves to the right, becomes straight or slightly curved with convexity to right.

The movements described in pathologic dilatations of the right heart are similar in nature to the normal movements noted during development of the fetus to maturity. In fact, they seem to be a continuation of the

same movement. Consequently it seems reasonable to state that as the right heart dilates the following changes occur:

1. **The heart and liver are displaced downward.**

2. **The right lobe of the liver is elevated with respect to the left lobe, the ribs, and the right heart.**

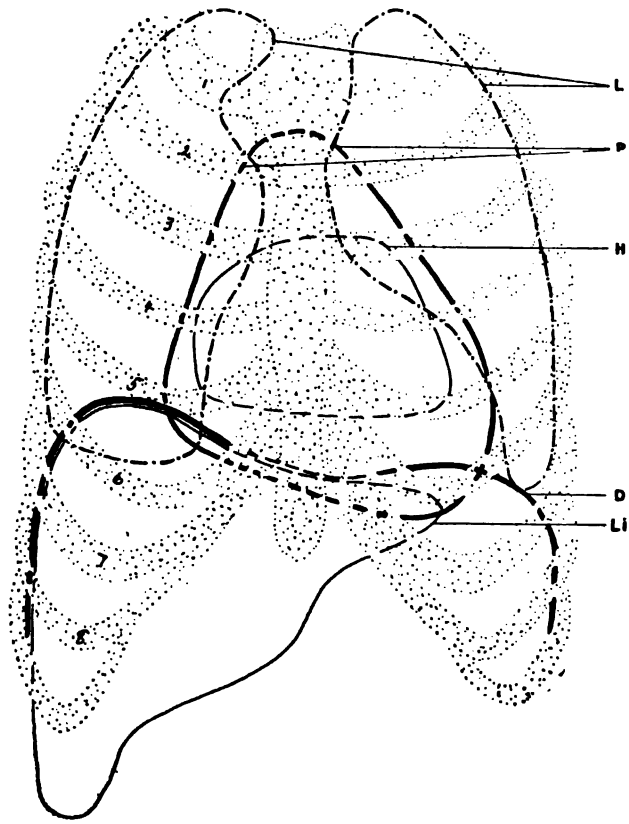

Fig. 3.—Pericarditis with effusion and dilatation of right heart (H); outline of pericardium (P) shown; liver (Li) at fifth rib, right lobe slightly higher than left; D, diaphragm; L, lung.

3. The inferior cava moves to the right, and its convexity to the right is increased.

4. The sternum and ribs are depressed. This depression of the ribs causes an apparent elevation of the right lobe of the liver, as high as fourth rib. This apparent elevation does not depend on the size of the liver.

In dilatation of the right heart the liver is actually depressed as measured by vertebræ, but apparently elevated as measured by ribs. As this changed relationship of the liver apparently depends on the same principles as the normal relationship of the liver, it is reasonable to assume that the apparent elevation (with respect to ribs) of the liver in dilatation of the right heart is constant; or a provisional general statement may be made, as follows: Dilatation of the right heart actually depresses the liver; the left lobe of the liver is depressed more than the right, producing a high cupolated right lobe; right lobe of liver due to depression of the ribs is higher than normal, apparent elevation; the degree of change in the form and position of the liver depends on the degree of dilatation of the right heart. Or the movement of the liver in markedly pathologic enlargement of the right heart seems to be a continuation of the normal movement occurring in the development of the fetus to maturity.

In pericarditis with effusion different physical forces are at work. Here the heart and venæ cavæ are compressed by the pericardial pressure and cannot dilate to the same degree as they do in the absence of pericardial pressure. The dilatation of the heart in pericarditis with effusion is most probably in many cases a postmortem phenomenon, developing as the autopsy progresses, and due to the congestion of blood in the large veins and lungs flowing into the heart as the pericardial pressure is removed. To be sure, the myocarditis present in pericarditis favors dilatation, especially if the pericardial pressure is low owing to weak pericardial walls. Again, the heart may be dilated before the effusion developed. In general, the physical forces in pericarditis tend to keep the heart at the same size as it was when the effusion began to develop, or at a diminished size. The inferior cava remains in its normal position or may be pushed to the left by the descent of the liver. The dilating pericardium extends to the right over the

diaphragm a distance depending on the degree of dilatation and the intrapericardial pressure tends to push the liver down. The degree of displacement of the liver depends, of course, on the degree of pericardial pressure. Here the liver has only its normal support.

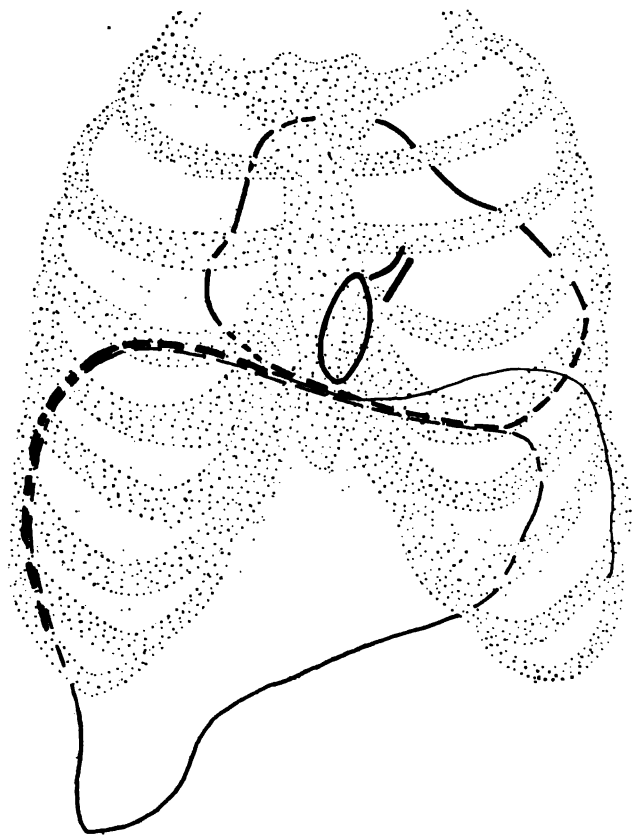

Fig. 4.—Aortic stenosis; right heart slightly dilated; liver very large and high.

The inferior cava remains near the median line in a posterior position. Consequently the right lobe of the liver is deprived of the support rendered in Case 1. In pericarditis with effusion the right lobe of the liver is displaced downward approximately the same distance as

the left lobe (without the apparent elevation as in cardiac dilatation). The right and left lobes of the liver are more nearly on a level or tend to assume the position found during fetal life. The sternum and ribs descend relatively the same distance as the liver. Here the liver is actually lower without the apparent elevation. A provisional general statement may be made as follows: Pericarditis with effusion tends to produce (or actually does produce) the following conditions: dimunition in the size of the right heart; actual depression of the liver without apparent elevation of the right lobe so that the right and left lobes are more nearly in the same plane; displacement of the inferior cava to the left with its convexity to the left. Or, in pericarditis with effusion, the relationship of the right heart and liver tends to revert to that found in fetal life.

It is thus seen that in the two conditions diametrically opposite physical forces are at work, the cardiac dilatation tending to produce a relatively high position, the pericardial effusion, a low position of the right lobe of the liver. A difference of as much as two or more interspaces in the position of the right lobe of the liver may occur.

Naturally the variation in the position of the normal liver is of importance. In the literature reviewed it seems that much of the material on which present statistics of the normal position of the liver is based is pathologic, and that the subject needs reworking with the pathologic positions of the liver and the type of thorax constantly in mind.

In cardiac dilatation the root of the right lung remains at about its normal level as compared to the vertebral column, and in Case 1 was on the upper, posterior portion of the left auricular wall. When the right auricle dilated the lower anterior portion of the right lung was lifted upward, outward and backward. The downward displacement of the ribs without a corresponding downward displacement of the right lung

gives an apparent elevation to the right lung. There is, then, an actual and an apparent elevation of the lower, anterior portion of the right lung.

In pericarditis with effusion, owing to the small left auricle, the root of the right lung is not displaced to a degree corresponding to that in dilatation. The lower, anterior portion of the right lung is not lifted as in dilatation, but pushed by the pericardial sac outward and backward. The downward displacement of the ribs gives an apparent elevation (if pleuræ are adherent the lung follows the ribs).

In cardiac dilatation the real elevation of the lower anterior portion of the lung border serves to diminish the area of lung-liver relative dulness. The degree of narrowing of this area varies from what might be called a diminished area to almost complete absence of relative dulness. The relative elevation of the liver places this area of dulness high, fourth rib.

In pericardial effusion the liver is pushed down proportionately more than the lower border of the lung is elevated, so that the area of lung-liver relative dulness is narrowed or obliterated and occupies a lower position than it does in cardiac dilatation. If the pericardial pressure is sufficient to push the sternum and ribs down the liver is also pushed further down, and consequently does not alter the relationship as described. Or, the differential sign should be, in cardiac dilatation, a high liver with a diminished area of lung-liver relative dulness, fourth rib; in pericardial effusion, a low liver with a diminished area of lung-liver relative dulness, sixth rib.

The differential sign is composed of two factors, the position of the liver and the presence and position of a diminished area of lung-liver relative dulness. Of these the position of the liver is most important, for the reason that it is more easily detected in corpulent patients in whom the lung-liver relative dulness may be too narrow for detection. The position of the lung-liver

relative dulness is more important than the fact that it is narrow. As the position of the relative dulness depends on the same forces which displace the liver the absence of or failure to find the relative dulness should not materially detract from the value of the sign. Owing to the physical forces causing the change in the lung-liver relative dulness this area must vary from a diminished area to an area of dulness too narrow for detection.

In cases of moderate cardiac dilatation and pericarditis with effusion the changes in the position of the liver and the lung-liver relative dulness cannot be developed to a degree sufficient for a clinical sign. But as the physical forces at play are essentially different in kind and effect these forces should develop in advanced cases a displacement of the liver sufficiently well marked to constitute a differential sign. As this sign becomes more and more marked as the lesions develop, it reaches its greatest development at a time when differential diagnosis is most difficult.

ABSTRACT OF DISCUSSION

DR. HAVEN EMERSON, New York: I believe that it is impossible to get the sign referred to with the patient in the dorsal position, or with the patient on his back on a table. In the dorsal position it is not possible to verify experimentally dilatation of the heart; but in the horizontal it is possible to verify by experimentation this condition in animals, the lower animals. What Dr. Calvert has presented to us should prove a very valuable diagnostic point if it could be verified by observation.

DR. W. J. CALVERT, Dallas, Texas: In the matter of experimental proof there are a number of difficulties to be considered. There is only one animal, so far as I know, having the same anatomic arrangement of the pericardium, namely, the monkey. Cardiac dilatation which causes a change in this relationship, it seems to me, must be slowly produced. There can be no question as to the sign that was produced; it was shown by cross section work on the cadaver, the section being treated with formol and reproduced. I have not had the opportunity to examine clinically many of these cases. I do not see how the position of such patients can materially influence the findings.

A CRITICISM OF THE BLOOD-PRESSURE APPARATUS

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The sphygmomanometer is generally assumed to be an instrument which enables us to measure the maximum and minimum endovascular arterial pressure. If this assumption is true, it does not follow that we have any data on which to estimate the mass movement of blood, the real problem that remains to be solved in the study of cardiovascular diseases. In subjects with a normal vascular system the blood-pressure apparatus gives us reliable information about the maximum systolic pressure. But in clinical experience it can be shown that the blood-pressure apparatus gives misleading information even on this basic point. The diastolic blood-pressure can be measured about as accurately as the systolic blood-pressure. But the diastolic endovascular pressure is not a measure of the systole of an artery. In other words, we may have the equivalent of a normal diastolic pressure and the artery remain full of blood during the cardiac diastole.

We are perfectly familiar with stasis in the centrifugal stream with high diastolic pressure as seen in chronic interstitial nephritis, but I doubt if it is generally recognized that we may have the equivalents of normal systolic and diastolic pressures and still have a marked stasis in the centrifugal blood-stream.

ESTIMATION OF DIASTOLIC PRESSURE BY SPHYGMOMANOMETER CONTROLLED BY PALPATION OF ARTERIES

Another point of interest I wish to discuss is the manner of estimating diastolic pressure in an artery and the reason for its reliability. Since the sphygmomanometer has been devised there seems to be a very general concession by clinicians that endovascular blood-pressure can be estimated only by instrumental means and that the older method of relying on the fingers is inaccurate and misleading. The source of error does not lie so much in the sense of touch as in the choice of the artery from which the estimate is made. I readily admit the impossibility of making an accurate estimate of blood-pressure from the radial or even the brachial artery. The only artery which serves this purpose is the femoral artery. The reason for this is very apparent. The femoral artery at Poupart's ligament is very accessible and lies on the pubes against which the artery can be compressed. Here we have an artery which gives us practically the lateral pressure in the abdominal aorta and lies under the mastery of the finger. When we palpate an artery, we do not feel the endovascular pressure, but we really feel the bursting tension of the arterial wall. The bursting tension on the walls of a hydraulic tube is equal to π R times the pressure, that is, 3.1416 times the radius of the tube multiplied by the pressure. This result is obtained by multiplying the circumference of the tube, which is 2 π R by the known pressure per centimeter square and then dividing the result by two. The product of the circumference and pressure must be divided by two, because the bursting tension would be equal to the pressure on one side only of any given diameter of the tube. Therefore, π R times the pressure equals the bursting tension in any artery.

If pressure remains constant, the bursting tension will vary directly as the radius of the artery. If we now assume the femoral artery to have a radius four times

that of the radial artery, it is quite apparent that any variation in pressure will be magnified four times in estimating the bursting tension of the femoral artery as compared with the bursting tension in the radial artery. This is analogous to the comparison between a microscopic view of 200 diameters and a microscopic view of 50 diameters. During the past four years it has been my practice to estimate the arterial pressure by palpating the femoral artery and afterward to use the blood-pressure apparatus. A little practice will enable one to estimate the blood-pressure very accurately. In pressures between 150 mm. Hg and 250 mm. Hg I find that there is rarely a disparity of more than 20 mm. between the digital and instrumental estimate, and as a rule the disparity is within 10 mm.

RESISTANCE OF ENDOVASCULAR BLOOD-PRESSURE AND HYPERTONIC VASCULAR WALLS TO PNEUMATIC CUFF

When very high pressures are recorded by the sphygmomanometer, the question has been raised as to whether the resistance offered the pneumatic cuff really represents endovascular pressure or the resistance of a hypertonic arterial wall plus endovascular pressure. The fact that supposedly high blood-pressures are often tolerated for years and with so little evidence of myocardial enlargement compels us to respect this criticism; but, on the other hand, when we have opportunity to study great oscillations of blood-pressure in a patient it seems very improbable that the resistance offered by the femoral artery should consist in wall resistance and the artery vary so little in volume during the periods of high and moderate pressure.

A year ago a patient at Lakeside Hospital had a blood-pressure which varied from 180 mm. Hg to 350 mm. Hg. These periods of hypertonus would last for several successive days and then subside. When the pressure registered as high as 350 mm. Hg in the arm, the resistance in the femoral artery was enormous. When

the pressure would again descend to 180 mm. Hg the femoral artery would feel slightly larger, but the difference in caliber could not have been great, for the variations in size of the femoral artery gave no hint of the change in pressure. If this great change in resistance of the arterial wall was due to resistance of a hypertonic wall and not to endovascular pressure we certainly had reason to expect great changes in the caliber of the vessels. This is always true in smaller arteries like the radial, where the proportion of muscular tissue in the arterial wall is much greater than in the femoral artery.

Since the arterial blood-pressure has been a subject of extended clinical observation, it has become apparent that either high endovascular pressure does not tax the heart so severely as we formerly believed or our measurements have been misleading, in so far as they have led to inferences regarding expenditures of energy in the output of the left ventricle.

REPORT OF CASES

CASE 1.—During the past winter a woman 50 years of age, who came under my observation, presented a very interesting problem in arterial pressure. The patient had not yet passed the menopause and had the appearance of being in good health. There is nothing in her family history or personal history which has any bearing on her present disability, except that the patient had always been a rather nervous person and for five years prior to the development of her first symptoms (which occurred eighteen years ago) she endured a great deal of worry and anxiety on account of the death of her husband and legal entanglements of his estate. Three years before the present attacks began, she found that in playing the piano her forearms became numb with a sense of tension, which was so uncomfortable and so persistent in its occurrence that piano-playing had to be abandoned. Fifteen years ago the first attacks of angina began. The pain begins between the shoulder-blades and runs about both sides of the thorax to the precordial area, and, when severe, runs down the inner side of both forearms. It is particularly severe in the right arm. These attacks of pain are accompanied by a sense of cardiac palpitation and eructations of gas from the stomach. The eructations of gas

are not, however, followed by any sense of relief. After the attacks there is a peculiar feeling of numbness in the hands, particularly in the right hand. Both hands are then hypersensitive to both heat and cold. There is never any dyspnea on exertion, although exertion will bring on the attacks of pain. Eating a large meal will produce the attacks, and often the patient is wakened out of a sound sleep by the pain. The patient's appetite is good, the bowels are slightly constipated.

The urine showed no indications of any renal involvement. There were no signs of any kind brought out on physical examination which betrayed any alteration of reflexes or any change in afferent or efferent nervous impulses. All diseases of the brain and cord or peripheral nerves could be excluded. The lungs, mediastinum, liver, spleen and alimentary tract revealed no signs of disease. The eye-grounds were normal.

The left border of the heart in the fifth interspace was 12 cm. to the left of the median line and the right border of the heart at the third interspace was 3 cm. to the right of the median line. The upper border of the heart was at the top of the third rib in the left parasternal line. The left border of the heart was not sensitive to direct percussion. I mention this because we very commonly find in the early stages of cardiovascular disease, when the myocardium begins to show some sign of distress, that the external border of the heart is marked by tenderness to direct percussion. This tenderness is not present in cardiac enlargement due to Basedow's disease, for in the early stages of Basedow's disease the cardiac enlargement is not associated with any impairment in the mass movement of blood. This tenderness is not present in cardiac enlargements of long standing, when due to either valvular or myocardial disease.

In our case, therefore, there was not a single sign of any kind which would indicate any impairment in the mass movement of blood. When the patient entered the hospital, there was perfect consistency between the feel of the femoral artery and the blood-pressure as registered by the sphygmomanometer applied to the arm.

The maximum systolic blood-pressure on entrance was 235 mm. Hg. The patient remarked that she had caused the bursting of every blood-pressure apparatus which had been used on her. The blood-pressure was first measured about two years ago and was then found to be 350 mm. Hg. The same high record was made by several physicians at different times. The highest pressure found during the patient's three weeks' stay in the hospital was 245 mm. Hg. Relief from the attacks of

angina has invariably followed immediately after taking 1/100 grain of nitroglycerin. The pains were so severe and relief followed so promptly from the use of nitroglycerin (which was always at hand) that we never had the opportunity to measure the blood-pressure during an attack, but I think it is fair to assume there was a marked rise in blood-pressure during the attacks of angina.

On February 18 the following experiment was made with nitroglycerin to see how much the blood-pressure could be lowered with nitroglycerin. A 1 per cent. alcoholic solution was used and the liquid was dropped on the tongue from a medicine-dropper.

Time, P. M.	Dose, Drops.	Pulse.	mm. Hg B.P.
9:30	1	75	215
9:32	1	72	...
9:34	1	76	224
9:36	1	81	...
9:38	1	81	238
9:40	1	84	...
9:42	1	84	234
9:44	1	81	...
9:46	1	81	208
9:48	2	81	...
9:50	2	78	162

In twenty minutes there were thirteen drops of a 1 per cent. solution of nitroglycerin given which was well tolerated. Nothing more than a slight sense of fulness in the head was complained of. The patient had the best night's sleep she had had for many weeks. The blood-pressure in the arm was never again as low as 162. This shows, however, that sclerosis of the artery could not have been a factor in resistance to the pneumatic cuff. There was no palpable thickening of any of the accessible arteries. An ophthalmic examination revealed no abnormality in the retinal nerve-heads or retinal vessels.

As soon as it was once learned that the blood-pressure could be reduced by the use of trinitrin without causing discomfort or any untoward symptoms, one drop of the 1 per cent. solution was given every hour and the dose was gradually increased in the course of three days to 5 drops every hour. The blood-pressure chart showed no alteration. The pressure was taken from the right arm every four hours. I then palpated the femoral artery and found the pressure nearly normal in that artery. The cuff was then applied above the ankle of the right side and the dorsalis pedis artery used for control. The artery was of fair size and quite as suitable for the purpose as the radial. Here the maximum pressure was only 160 mm. Hg. The blood-pressure apparatus nearly always gives a higher registration when applied to the leg, so it seems fair to assume

that this measurement would be consistent with an arm measurement in the average normal subject of about 20 or 30 mm. less. The cuff was then applied to the left arm and the pressure measured there was slightly less than in the right. Here is a patient with a history of vasomotor angina with blood-pressure of 245 in the arms and 160 in the legs after trinitrin had been given in large doses. The pressure in the femoral arteries prior to the administration of nitroglycerin was consistent with the pressure in the arms; now, however, the femoral and brachial arterial pulses did not feel as though they belonged to the same person.

If it is possible to have widely differing blood-pressures in branches of the aortic system, then it is apparent why this patient, whose brachial pressure was so high for two years (of which we know), revealed no signs of distress in the heart. If the splanchnic arterial distribution constantly maintained the same low pressure, compared with the accessible arteries, as the femoral artery now shows, compared with the brachial, then it is quite apparent that the brachial pressure did not habitually represent the pressure in the thoracic aorta and for this reason the myocardium showed no signs of distress after years of supposedly high pressure.

Another explanation of myocardial preservation under such conditions was suggested by the history of another patient who was first seen in 1905.

CASE 2.—The patient, a man, then 35 years old, had marked cardiac hypertrophy, high arterial pressure and pulmonary edema. Rest in bed, milk diet, warm baths and nitroglycerin gave him great relief. After a month of this treatment he left the hospital and was not seen again until four and a half years later, in 1909, when he again presented himself with the same symptoms, although not quite so severe as four and a half years before. It was then learned that he had continued uninterruptedly at his vocation of barkeeper, that he had been quite comfortable during all that period, and that he had taken nitroglycerin for only a few weeks after his first stay in the hospital. We then found that his blood-pressure on waking in the morning was only 130 mm. Hg, and in half an hour it would again be 190 mm. Hg, where it obstinately remained in spite of the use of nitroglycerin. There was never any disparity between the feel of the femoral pulse and the brachial

pulse in this man, but the pressure in the leg was not taken with the instrument. It was found later that if the blood-pressure was taken immediately when the patient awoke from a short nap of thirty minutes, it was only 130 and regained its original point of 190 about one-half hour after waking. These observations were made repeatedly in this man on waking in the morning and on waking after short naps and the results were always the same.

This patient, therefore, had an arterial hypertonus when awake, and vascular relaxation when asleep. What preserved him so long against myocardial exhaustion was the slumber relaxation. This amounts to a very great compensatory measure in a man who gets nine hours' sleep every day. To return to the first patient, however, it was found that she did not at any time have a lowered blood-pressure on waking; and furthermore her attacks of angina often came on during sleep; consequently, we can eliminate slumber relaxation as a compensatory measure in her case.

The other problem which presents itself is whether the patient really had such widely differing pressures in the femoral and brachial arteries or whether the hypertonus of the artery offered the resistance to the pneumatic cuff. Were we really measuring resistance of a hypertonic arterial wall and not endovascular blood-pressure? Three resident physicians at Lakeside and I tried exposing an arm to extreme cold to see if the pressure in the exposed arm differed from the pressure in the other arm which was not exposed to cold. The experiment was made in the following manner:

The person under observation lay flat on a table with a trough of ice-water at his side. A blood-pressure apparatus was applied to the left arm and to the right arm at the same time and the pressure recorded. Then one arm was laid in the ice-water and, when the arm became painful from extreme cold, the pressures in both arms were recorded. In the other three men there was no essential change, but in my own case there was a marked rise in pressure in the cold arm and no rise in the other arm. The pressure in my right arm was 136 and in the left arm 126. Then the right arm was laid in the

ice-water so that the upper arm as high as the top of the cuff was covered. When the arm became very painful, the pressure in both arms was measured. The left arm recorded 126 as before but the maximum pressure in the right arm was 158, a rise of 22. There could have been no error in palpating the radial artery, because I could tell the instant the least trickle of blood passed beyond the cuff by the feel of the water-hammer jet, which could be perceived equally well when the arm was in and out of the water. The instant the arm was lifted out of the water and the pain ceased, the pressure was again lowered to the original point of 136.

On another occasion I tested my blood-pressure much in the same manner, but under different conditions. The early part of the day from 9 to 11.30 a. m. was occupied in making a ward visit, from 12 to 2 p. m. was occupied with writing, then a moderate luncheon, at which two cups of tea were drunk, was followed by smoking one cigar. An hour later the experiment was made. The pulse-rate was 72 per minute. A blood-pressure apparatus was applied to each arm and the records were made by two resident physicians. One man watched each apparatus and recorded their results independently of one another. Before the right arm was put in the ice-water the maximum systolic and diastolic pressures, respectively, were 170 and 133 in the right arm and 168 and 132 in the left arm. The femoral artery was then palpated by Drs. McLaughlin and Boyer (who are experienced in estimating blood-pressure) and both agreed that, when the one arm was put in cold water, a decided rise in pressure was perceptible, which was consistent with the records made by the instrument. Several trials showed a rise to 180 in the chilled arm. It does not seem likely that the rise in pressure was due to pain, for, though the three other men experienced quite as much pain, their pressures did not rise after exposure to cold. On both occasions when the observations were made, the exposures to cold were made repeatedly. On the first occasion there was a rise only in the chilled arm and none in the other arm. The second trial showed a consistent rise in all accessible arteries. The rise was both in the systolic and diastolic phases. The disparity between the pressure in different arteries in the case of one patient was apparent only after trinitrin was used in considerable dosage, but this disparity was confirmed by repeated examinations during a period of a week. The differing results in my own experiments with the cold water were just as certainly established by repeated measurements.

Whether there were really different endovascular pressures in the several arteries, or different degrees of hypertonus in the arterial walls which gave the results, the deduction remains the same, namely, that the blood-pressure apparatus applied to accessible arteries does not give infallible information as to the aortic blood-pressure and, as a consequence, it is not safe to rely on routine measurements from the arm as a guide to the employment of vasodilators in treating patients with high arterial pressure.

The maximum systolic and minimum diastolic pressures may be within the normal limits and still the mass movement of blood be much impaired. Recently I observed a ward patient at Lakeside Hospital who had pronounced cardiac dilatation and tricuspid insufficiency, as evidenced by dilated jugular veins with a systolic centrifugal pulse, which was plainly seen in the jugular veins and was distinctly palpable in the liver, which was enlarged a hand's breadth below the costal border. The patient had general edema and very marked cyanosis and orthopnea. The pulse-rate was 90, the maximum systolic pressure in the arm was 135 and the minimum diastolic pressure 96. That there was a severe alteration in the mass movement of blood in this patient was clear enough from the cyanosis, dyspnea, venous and hepatic pulsations and edema of the lower extremities.

Although the maximum systolic and minimum diastolic pressures were equal to those we often find in patients with a good mass movement of blood, palpation of the arteries revealed an artery filled with blood during the diastolic phase. There was, then, an increased resistance in the peripheral arterial distribution and stasis in the centrifugal arterial stream without an elevation in either the systolic or diastolic pressure. With these arterial conditions, then, there must be a small ventricular output with each ventricular systole. A very small ventricular output is sufficient to elevate the pres-

sure to moderate height (135 mm. Hg) in an arterial system which is full of blood at a moderate pressure during the cardiac diastole. This patient's myocardium was the factor which was chiefly at fault in the circulatory system. As a rule, patients with an increased peripheral resistance in the arterial system have high systolic and diastolic pressures, but, when the myocardium becomes inefficient at the same time that the increased arterial resistance develops, the systolic and diastolic pressures remain the same as in health, but the mass movement or minute volume of blood is greatly diminished.

If reliance is placed on the blood-pressure during systole and diastole, as a guide to the state of the circulation one can be greatly misled, for the pressure measurements are of value only when they are contemplated in the light of other evidence, which must be gained by observation.

DETERMINATION OF MINIMUM DIASTOLIC PRESSURE BY BLOOD-PRESSURE APPARATUS

Finally, I wish briefly to discuss the blood-pressure apparatus as a means of determining the minimum diastolic pressure. The two methods employed are (1) to find the pressure-point in the pneumatic cuff at which the mercury column has a maximum excursion, and (2) to find the point at which the sound heard distally to the cuff, suddenly diminishes in intensity, as the pressure in the cuff is gradually lowered. The first method is much less satisfactory than the second method. It is the second method which has some points of interest in the physics of the arterial circulation. If the brachial artery is compressed against the inner surface of the humerus, and the bell of a stethoscope is applied over the artery a short distance below the point of compression, there will be, of course, no sound audible so long as the artery is obliterated during cardiac systole. On diminishing the

pressure so that a jet of blood escapes under the compressing finger, there will be a murmur and sound audible during the heart's systole, but the murmur predominates and often the sound is scarcely perceptible with the murmur. If a pneumatic cuff is applied and the pressure in the cuff is diminished so that a jet of blood escapes under the cuff during systole, but not during diastole of the heart, the relative intensities of murmur and sound are reversed. The sound, which is very like the "pistol-shot" tone, is loud and the murmur is faint. In many cases the murmur is not audible and only the pistol-shot tone is heard. If the femoral artery is compressed at the pubes, the so-called stenosis murmur is very loud and the pistol-shot tone is not heard at all. If one compresses the femoral artery, however, and then very cautiously relaxes the pressure so as to permit the very smallest possible jet to escape under the finger a pistol-shot tone is heard unaccompanied by a murmur, but, unlike the case with the brachial artery, when a larger jet is allowed to escape by relaxing the pressure a very little more a loud murmur is heard without the pistol shot tone. The sharply defined pistol-shot tone is heard only a short distance below the cuff or compressing finger in all instances.

The conformation of the jet seems to determine whether a murmur or pistol-shot tone will predominate. Flat compression of the artery gives, in all probability, a different contour to the narrowed lumen from that procured by the circular pneumatic constriction. In the latter case the compression is applied in a number of different radii, whereas, in the former case, only a narrowed chink can be formed. Probably, as the constricted lumen more nearly assumes a circular contour, the water-hammer effect is more in evidence and the murmur is wanting. When the pneumatic cuff is used, in many cases only a pistol-shot tone is heard and no trace of a murmur is heard. When the brachial artery is compressed by the finger, a murmur is always audible

and predominates, whereas the pistol-shot tone is comparatively faint.

Another point about this pistol-shot tone is of interest. Suppose we have a maximum blood-pressure of 150 and a minimum pressure of 100. The pistol-shot tone below the constricting band will have attained its maximum, when the cuff pressure is at about 145, and will remain at the same intensity until the pressure in the cuff is just high enough to prevent the escape of fluid during the heart's diastole. Then when the pressure in the cuff is no longer high enough to shut off the centrifugal flow during diastole of the heart, the sound becomes faint, so that the pistol-shot tone will grow faint immediately when the cuff pressure goes below 100. The pistol-shot tone is due to the escaping jet of blood and not at all to the excursion of the collapsed arterial wall below the cuff. As the pressure in the cuff is diminished, the arterial lumen under the cuff increases; consequently, with a diminishing pressure in the pneumatic cuff the volume of the jet increases, but the velocity will diminish. Therefore, the mass times the velocity in the jet remains constant, until a point is reached at which a null pressure in the artery distal to the cuff no longer exists during cardiac diastole, and then the difference in pressure, above and below the cuff, is no longer great enough to produce the water-hammer effect.

I attempted to reproduce these phenomena by inserting a cannula in the subclavian artery of a fresh cadaver. The radial artery was opened and the cuff of a blood-pressure apparatus applied to the arm. Liquids of varying specific gravities were pumped through the artery, when the pressure in the pneumatic cuff was at varying points from 120 to 300 mm. Hg, but the pistol-shot tone could not be produced and the pulse of the jet of liquid, as it shot beyond the constricting cuff, was very different from the pulse of the jet of blood during life. Instead of the high velocity with which the jet

of blood during life shoots under the cuff, there was a lazy rise and fall in the pulse below the cuff. No pistol-shot tone was heard; nothing but a murmur was audible with all the pressures and kinds of impulses we were able to give the jet of liquid. It would evidently require a nicely constructed power-pump to produce the same kind of jet which occurs in the blood-stream during life.

When air instead of liquid was pumped through the artery, the velocity of the jet was of course much greater and the pistol-shot tone immediately below the cuff was very loud. When a bandage was drawn about the forearm at the same time that air was pumped through the artery, the intensity of the pistol-shot tone diminished, as very slight pressure was applied by the constricting bandage. As soon as the pressure of air in the artery between the cuff and the bandage no longer sank to zero between the impulses from the pump, the pistol-shot tone diminished in intensity.

When the brachial artery immediately below the cuff was exposed and opened and traction applied by means of two forceps so as to eliminate the factor of excursion of the arterial wall, the pistol-shot tone below the cuff remained the same as before.

CONCLUSION

I do not wish to discourage the use of the blood-pressure apparatus. It is a very valuable instrument, but its chief value consists in teaching us how to palpate the arterial pulse. No instrument can take the place of the finger, nor can any instrument teach as much about the pulse as can be learned by palpation.

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ABSTRACT OF DISCUSSION

DR. JUDSON DALAND, Philadelphia: We owe Dr. Hoover a debt of gratitude for calling attention so plainly and definitely to the facts, not generally remembered, that the blood pressure varies at different times of the day, and more particu-

larly, in certain cases, and that there is a difference between the blood pressure in the waking and sleeping states. Again, the mere application of the pneumatic cuff in certain neurotic subjects often increases the blood pressure as much sometimes as 30 or 40 mms. Often the fainting patient will permit of a true reading. Observation systematically made will show in many instances a temporarily extraordinary increase in the blood pressure. Therefore, it seems to me that we should bear in mind that variations occur in many cases. The case reported by Dr. Hoover, so far as I know, is a very unusual one; I have no recollection of any such experience in my practice, nor do I recollect any such extraordinary disparity between the blood pressures of the inferior and superior extremities. So far as the determination of the blood pressure by means of the finger applied to the radial artery is concerned, I have found that in about three-quarters of the cases I can estimate approximately the blood pressure; but in the remaining 25 per cent. I am at sea. We should thank Dr. Hoover for calling our attention to the femoral artery where manifestly there is offered a physical condition vastly superior to the radial artery.

PATHOLOGIC RELATIONSHIP OF ULCER AND CARCINOMA OF THE ALIMENTARY CANAL

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INTRODUCTORY

Any line of investigation which promises assistance in combating the spread of cancer is worth while. For, discounting to the utmost government census figures everywhere, there yet remains the facts, first, that cancer is increasing materially in relation to the total number of deaths from all causes, and, second, that it is increasing materially in relation to the total number of living. Speaking broadly, it is probably increasing more rapidly than any other of our diseases. And this increase is greatest in the most prosperous nations and in the most prosperous classes within such nations. Further, it attacks individuals at their highest productive period. It attacks particularly the primary organs of perpetuation of the individual, i. e., the reproductive apparatus. In the male approximately two-thirds and in the female one-fourth of all cancers develop in the alimentary canal, while one-half of all cancers of the female are in the reproductive organs.

It seems to us that in our consuming interest in the initial excitant or ultimate cause of cancer, there is a possibility of our losing sight of the importance of the study of the tissue conditions of the affected individual.

When the relationship of bacteria to infectious disease was first brought to the attention of the scientific world for a long time the specific germ was the chief object of study. Experience soon taught us, however, that in combating infectious diseases it is even more important that we familiarize ourselves with those conditions of the body by which nature combats disease. We are apt to forget that if we knew to-day the primary irritant in carcinoma as well as we know the leprosy bacillus we might still be almost as helpless as we now are in controlling the disease. We would still be under the necessity of investigating most carefully the anatomic and physiologic condition of the tissues which permit the primary excitant, whatever its nature, to become effective.

CLINICAL EVIDENCE

From the purely clinical standpoint, probably the most salient points which present themselves in relation to tissue susceptibility to carcinoma are the following:

1. Carcinomata of the reproductive organs in the female—one-half of all cancers in this sex—occur principally at the age when the reproductive organs have begun their regressive changes.

2. Carcinomata of the alimentary canal—two-thirds of all cancers in the male—follow in the great majority of cases chronic non-cancerous irritation.

ANATOMIC EVIDENCE

When once removed from the body, tumors of the alimentary canal are of relatively easy study, because of the comparatively simple anatomic relationships; the thin walls with well-defined laminæ and simple glands. The lips, mouth and anus are, of course, exceptions to this. When we examine carcinomata of the alimentary canal we find them in a great majority of cases developing on epithelial tissue which has been displaced either by ulcerative changes or by diverticula. An ulcer of the mucous membrane of the alimentary canal shows within

its base usually only granulation tissue, all of the tubular glands having been destroyed. At the margin of the ulcer is an overhanging border consisting of hyperplastic mucosa. Where this hyperplastic area meets the eroded base is a ring in which are found islets of tubular epithelium which have been cut off from their connection with the outer world by bands of scar tissue.

The center of the ulcer, filled with granulation tissue, is almost always on a level with that of the normal base of the mucosa, within which is the ring containing segregated epithelium. The tendency of such islets of segregated epithelium is toward destruction by the cutting off of their blood-supply by scar tissue. In a careful study of these cell inclusions, however, we frequently find that many of the islets instead of degenerating show more or less proliferation of their cells. This is evidenced by their apparently increased number in a cross-section, by their mitotic figures and their dividing nuclei. Such inclusions are of frequent occurrence around the borders of all ulcers of the stomach, duodenum, gall-bladder, appendix and large intestine. It is probable that the proliferation of the epithelium within such inclusions is frequently stopped by the cutting off of the blood-supply, and that degeneration results. When, however, we study many lesions of this type, particularly within the stomach, we find that certain groups of epithelium show not only proliferation of their cell contents, but that the proliferating cells are infiltrating the surrounding tissues; that this is a true passage of the epithelium into the previously formed scar tissue. That the picture is not due to the presence of remains of included epithelium which has been only partially cut off from its normal site there can be no doubt in the mind of one who studies the sections with proper care. The epithelial cells which are insinuating themselves between the bands of fibrous tissue are not old degenerating cells, but are cells which are proliferating, as is shown by their staining reactions and their dividing chromatin. It is note-

worthy that this proliferation is usually most marked in the portion of the epithelium-bearing ring which is furthest removed from the center of the ulcer with its scant nutrition. More than 70 per cent of all of our cancers of the stomach give satisfactory gross and microscopic evidence of previous ulceration and isolation of epithelium, while the evidence is equally clear in our cancers of the gall bladder. We have seen at no point within the alimentary canal any evidence that surface irritation, however prolonged, has anything to do with providing conditions suitable for the development of carcinoma. It seems to be a *sine qua non* that the portions of epithelium shall be displaced from their normal relationship, and this does not occur where superficial irritation alone is concerned, but only in ulcers and diverticula.

The relationship of small diverticula of the alimentary canal to carcinoma has not been fully appreciated, partly because the presence of the diverticula themselves have been but recently called to our attention. When Drs. Mayo, Giffin and Wilson placed on record our five cases of diverticulitis of the sigmoid three years ago, there were on record only eighteen previous cases. One of these presented a carcinoma of a diverticulum. The number of cases of diverticulitis has increased during the subsequent three years until there are now on record nearly one hundred cases. We have added five new ones to our list. In these five two are cases in which the operation was made primarily for well advanced carcinoma and diverticula were found in the base of the carcinoma. The epithelium within small diverticula is frequently quite as completely occluded from connection with the interior of the viscus as is that lying at the base of an ulcer of the stomach. Here, as in the isolated islets of epithelium within the stomach, the tendency of the segregated cells is to degeneration from reduced nutrition. They do, however, occasionally proliferate

greatly and, as we have shown in three of our nine cases, they may also infiltrate and thus form carcinoma. When one goes over a number of cases of carcinoma of the sigmoid one is struck with the patch-like or ring-like character of all of the lesions, except those of the most advanced type. This is exactly the sort of tumor which one would expect to find developing on isolated epithelium within diverticula, and the two tumors whose origin, as we have demonstrated, has been on diverticula, are of exactly this type. In order to show the presence of diverticula in carcinomata of the sigmoid which have advanced to any extent, it is necessary to use the utmost care in examining the specimen while it is still fresh.

Sometimes with fresh specimens this can be done by very gently probing from the inner side of the tumor, or better still, by carefully slicing off the tumor from the serous surface and parallel thereto, and examining underneath each slice as it is removed. We are satisfied from our experience that many cases of carcinoma of the sigmoid and rectum have had their origin on divertic ula which have been overlooked at operation, even when they were still undestroyed by the tumor.

In the last 5,000 appendices which have been removed at our clinic we have discovered twenty-two primary carcinomas. In reviewing these recently, Drs. MacCarty and McGrath have noted that all of these tumors have occurred in the tips of appendices which had been previously obliterated. This obliteration in all cases extended well proximal to the tumor, and showed the formation of scar tissue at some point proximal to the tip in greater quantities than in the tip itself. The glandular epithelium of the tip of the organ has been separated from the lumen of the caecum. Such epithelium is frequently found to show hyperplasia or adenomatous proliferation. In the twenty-two cases which we have found, however, there is much more than this, viz., an

infiltration of the deeper layers of the appendix, resulting in unmistakable primary carcinoma.

In the tough fibrous stroma of the border of the lips it is difficult to make out microscopically any evidence of flat-cell inclusions. The lips of practically all adults have been so frequently subjected to traumatic scars, ulcers, etc., as the result of nutritional disturbances that it would seem probable that such inclusions of the epithelium are frequently present. Carcinomas of the lip, however, usually come to the clinic so late that all microscopic evidence of their previous benign ulceration has disappeared, though the clinical histories recite such evidence in an unmistakable manner.

Within the mouth the relationship of ulcerating leukoplakia to subsequent carcinoma is established on a very firm clinical basis, though here, as in carcinoma of the lip, the patients most frequently come to operation at a period when all microscopic evidence has been swallowed up in the advance of the secondary disease.

To summarize, then, the results of our studies, we may say that in the alimentary canal, whatever may be the essential irritant—micro-organisms, ferment or what not—the fact remains that in a very high percentage of the cases there is microscopic evidence backing up clinical evidence that the carcinomata have developed on epithelial cells which have been previously isolated from their normal surroundings, either by the formation of diverticula or by being cut off by scar tissue in ulcer bases. This statement has in it neither support nor contradiction for any hypothesis as to the character of the essential irritant in carcinoma. Just as we must have tissue cut off from sufficient blood-borne oxygen in a punctured wound in order to permit development of the tetanus bacillus, so it seems that in the alimentary canal we must have tissue which is cut off from its relationship with the outside world in order to have the develop-

ment within it of whatever may be the essential irritant of carcinoma. Whether this isolation of epithelium is a primary necessity for the formation of carcinomata throughout the body is another question. Certain it is that a similar condition exists in the female breast which is undergoing regression. Certain it is that similar conditions exist in the uterus, with its partially shed epithelium, with its frequent erosions, and with its regressing mucosa. Certain it is that a similar condition exists in the prostate as the result of inflammatory changes segregating islands of epithelium. Within the kidney true carcinomas are frequently associated with the ulcerated process secondary to nephrolithiasis, while the so-called "hypernephromata," on the other hand, are apparently the result of the proliferation of tissue which has failed to become connected embryologically with the portion of the tubular epithelium which is in direct relation with the renal pelvis. Indeed, as we look over the whole field of carcinomata we must agree with Adami that these tumors are the result of the development on either postnatally or prenatally displaced cells which exhibit a tendency to revert to the embryonic type.

The clinical bearing of all of this is in teaching the importance of the recognition and cure of those disease processes which, however benign in themselves, tend to isolate epithelium. There can be no question but that chronic ulcers of the mouth should be promptly cared for. Ulcers of the stomach should receive the most minute attention. The obliterating appendix, however innocent its look, should invariably be removed when found. Diverticula of any portion of the large intestine should be treated by complete removal rather than by a drainage of the abscesses which may be formed about their extremities. The greatest difficulty of course is in the early diagnosis, but that is without the province of this paper.

PATHOLOGIC MATERIAL STUDIED

167 cancers of lip.
46 cancers of mouth and tongue.
2 cancers of esophagus.
189 cancers of stomach.
15 cancers of gall-bladder.
22 cancers of appendix.
20 cancers of cecum.
42 cancers of remainder of colon.
67 cancers of rectum.

570

SUMMARY

Of the cases of cancer of lip 30 per cent. gave evidence of previous isolation of epithelium.

Of the cases of cancer of stomach 67 per cent. gave such evidence.

Of the cases of cancer of gall-bladder 33 per cent. gave such evidence.

Of the cases of cancer of appendix 100 per cent. gave such evidence.

Of the cases of cancer of cecum 10 per cent. gave such evidence.

Of the cases of cancer of colon 40 per cent. gave such evidence.

Of the cases of cancer of rectum 3 per cent. gave such evidence.

CONCLUSIONS

1. The relationship to cancer of simple chronic irritation of the unbroken free surface of the mucosa of the alimentary canal, as indicated by clinical data, is not readily demonstrable pathologically.

2. Scar tissue at the bases of ulcers, obliterations of the lumina of appendices, and diverticula segregate portions of mucous epithelium from the neighboring epithelium and from the lumen of the alimentary canal.

3. These portions of segregated mucous epithelium tend (a) to degenerate from pressure and diminished blood-supply, or (b) to proliferate and infiltrate the surrounding tissues, thus forming cancer.

4. These islands of segregated epithelium probably should be regarded as points of least resistance only, and requiring the presence of other factors for the production of carcinomata.

ABSTRACT OF DISCUSSION

Dr. H. E. Robertson, Minneapolis: We are all helpless in the presence of cancer. Sometimes we believe that malignant growths are preceded by absolutely normal structures; this morning we have had another view presented. Dr. Wilson's contribution is of great value in showing specimens which demonstrate at least one phase of the problem. The activities of epithelial cells may be grouped under two classes: first, that of function, such as secretion or absorption, and second, that of manipulation or proliferation. When for some reason or other the functional activity is checked, all the inherent capacity of the cell may be directed toward wild, uncontrolled proliferation. Such a process might be supposed to be working in ulcers and inflammatory conditions which in all probability precede many carcinomatous tumors of the gastro-intestinal tract. The functional activity is inhibited because of inflammation, and some of the cells continue to multiply unchecked by any normal balance. I do not believe that Dr. Wilson would, for a moment, claim that all cancers arise from ulcers or preceding inflammatory lesions nor would he give the impression that all ulcers of the digestive tract gave rise to carcinoma. His paper emphasizes what we have beeen taught for many years, namely, that some ulcers of the gastro-intestinal tract may show cancer arising on the old margins.

Dr. J. N. Hall, Denver: I wish to speak about the diagnosis of certain conditions requiring gastro-enterostomy for pyloric obstruction, and I base my remarks on a series of 71 cases in which ulcer has been found blocking the pylorus. In these cases, the patients were operated on by Drs. Freeman, Perkins, Craig, Lyman, Fleming and other Colorado surgeons. During the same time a diagnosis of peptic ulcer was made in 81 other cases, and a very probable diagnosis in 23 cases, 175 cases in all, indicating that 40 per cent. of my cases of ulcer seemed to me and to surgeons doing much of this work, to need gastro-enterostomy. I exclude here all cases of ulcer operated on for perforation or in which resection was done because of the probability of cancer, and all gastro-enterostomies done for cancer, congenital pyloric stenosis, etc. So far as I know, there is no exact parallel for the state of affairs which exists as to this diagnosis. Many physicians recognize the gastric ulcer which blocks the pylorus, whether it be by producing spasm, by its thickening effect on the mucosa, or by the production

of scar tissue. But for every clinician who frequently sees these cases there are ten who practically never call on the surgeon for help in treatment. These men either do not recognize the condition or do not recognize the fact that surgical intervention is demanded. Yet many surgeons diagnose these cases and operate without either the professional assistance or the normal support of the internist. It is a strange fact that the surgeon in many of these medical cases makes a better diagnosis than the physician. A surgeon of one of the oldest and most famous hospitals in America told me a few weeks ago, when I inquired as to the treatment of pyloric obstruction, that he was ashamed to tell me how limited his experience was, since the medical men of that institution practically never referred such cases. Yet in that city another surgeon at another hospital does much of this work. There is much ground for criticism of the profession in that so much stomach work is done by so many men, but a small proportion of whom recognize the frequency of this condition, its ease of diagnosis, in most cases, the almost certainty of relief by surgical help, and above all the overwhelming evidence that the end of these patients is slow starvation or eventually cancer. From Rochester we learn that 71 per cent. of resections for cancer showed origin in an ulcer, and 68 per cent. of the resections for ulcer showed cancerous changes. Yet under the diagnosis of dilated stomach, atonic dyspepsia, gastralgia, gastrodynia, nervous prostration, etc., these patients go on toward starvation or cancer, or both. In 11 of my cases the ulcer had evidently existed for from 18 to 30 years.

While the medical men discuss the fine points of differential diagnosis, some good surgeon, or a medical man who stands daily by the operating table and sees what the living pathology of the abdomen reveals in the cases he refers to the surgeon, often intervenes and by timely operation restores the patient to health.

We found associations for the study of cancer, but allow patients with ulcer of the pylorus, the very mother of cancer, go on under treatment by alkalies, bismuth and pepsin, the latest diet, etc. knowing all the time that cancer of this region kills more people than any other form, that it is curable by operation under favorable conditions and by operation alone. I go so far as to say that I am convinced that pyloric ulcer is so likely to lead to cicatricial stenosis, if it ever does heal, or to cancer if it does not, that I personally would not submit to any but surgical treatment for such a condition, nor do I recommend prolonged medical treatment to my patients. And yet such is the conservatism in certain quarters that if a patient with dilated stomach escapes from the internist and is cured by the surgeon, the internist will almost say, as did the arrogant Viennese professor of 50 years ago when one of his patients to whom he

had given a fatal prognosis recovered under a new line of treatment at the hands of one not a university professor: "You must have been treated wrongly."

Dr. Frank Wilbur Foxworthy, Indianapolis: I am an internist and I want to know the relationship between ulcer and cancer in relation to time; how much time elapses from the ulcer stage? I have under my care an old woman with ulcer near the pylorus of five years standing. She was on an albuminous diet for 6 weeks and then left the hospital free from symptoms for 13 months and she now weighs 168 pounds. Am I to believe that she is in danger of developing cancer or to suffer from the thoughts of expecting it the rest of her life?

Dr. D. C. Walt, Little Rock, Ark.: I should like to emphasize a point which I think might be of interest to physicians as well as to surgeons and showing that we should know our limits. I have had an epithelioma, and I feel that I have been benefited both by the general management of my case as well as by the use of the *x*-ray which was applied by a Chicago physician. I feel that I am fresher to-day than I was ten years ago, and I do not attribute it all to the *x*-ray. Every cell organism, every animal organism is dependent on a general law, for its building process; it is a matter of waste and repair, of supply and demand. When we wait until the cell is dead, whether it is from abscess of the liver or in the tubule of the kidney, or carcinoma, the cell is dead and dead forever. We as animals, have attempted to interfere with Nature's method of living. Think of the results produced by our notions which interfere with Nature's laws of waste and repair. When the child is born, the mother places a napkin on it, making a barrier to elimination. When the child becomes older he is harnessed more securely and by the time he is matured he thinks he is living within Nature's law. One man develops arteriosclerosis, another carcinoma, another tuberculosis, all coming under the disturbances of waste and repair. We must recognize sympathetic nerves and their power to control the physical conditions, when properly influenced by the electromagnetic power.

Dr. Charles G. Stockton, Buffalo, N. Y.: I feel that I ought not to allow the remarks made by Dr. Hall to go without some reply. It seems to me that his attitude toward the physician and the internist in the matter of treatment of acute ulcer as well as of chronic ulcer is wrong. I have no doubt at all that we do sometimes find cancer growing on the seat of a chronic ulcer; this certainly does occur, but not so often as one would infer from Dr. Hall's remarks. I have studied peptic ulcer carefully for years and I have had recurring cases under observation for many years and they did not develop into cancer. Furthermore, it is unnec-

essary in the majority of these cases of ulcer of the pylorus to resort to surgical treatment except in cases having definite and positive indications. It is unfortunate that so much importance should be attached to the scar tissue; it is unfortunate that anyone should take the position that when there is a scar as the result of a gastric ulcer, the case should go to the surgeon, because it often results in the subsequent ill health of the patient. If the cases were selected by discriminating men, if only skilful surgeons operated in such cases, we then might go further and advise operation oftener. But I have seen so many evil results from the employment of surgical methods on this part of the economy that the statements made by Dr. Hall seems to me misleading.

Dr. Richard Weil, New York: It seems to me somewhat questionable to interpret every instance of epithelial segregation or inversion as evidence of a tendency to carcinomatous degeneration. The presence of granulation tissue seems, as a rule, to carry with it a stimulus to this very sort of atypical epithelial proliferation. Consequently it is not a rare concomitant of chronic inflammatory processes in various parts of the body. Fisher and others have been able to produce similar results by means of chemical irritants, such as scarlet red, but they have not nevertheless produced true cancers. Occasionally, of course, cancer may originate in this fashion, but to assert on the basis of these microscopic changes that the majority of ulcers show a tendency to carcinomatous degeneration is an altogether different matter.

Dr. John A. Lichty, Pittsburg, Pa.: The pathology which Dr. Wilson has shown us to-day is convincing, and I believe that he has established his point. I am led to recall, however, the appearance of uterine scrapings which have been looked on as suspicious of a beginning carcinoma. In some of those cases I have sent sections to the pathologist—in one case in particular to Dr. Welch, of Johns Hopkins—which, to me, looked suspicious; yet Dr. Welch told me it was not malignant, and explained the condition very much as Dr. Weil has attempted to explain some of the lesions which Dr. Wilson has demonstrated. The subsequent history of these cases confirmed Welch's opinion. I am afraid Dr. Hall has drawn conclusions from Dr. Wilson's paper which are not relevant to the subject. I do not believe that in all cases of gastric ulcer, and those suspicious of gastric ulcer, the abdomen should be opened and the ulcer incised. This would lead to a great amount of unnecessary surgery and would expose patients to a great risk.

It will be recalled that in only 20 of the 5,000 cases of appendicitis was malignancy found. Now, we know, of course, that malignancy in the stomach is more frequent than in the appendix. I can agree with Dr. Wilson's con-

clusions as he has stated them, but I would not be willing to attach the conclusions which Dr. Hall has presented to us this morning.

Dr. A. Jacobi, New York: All of us I believe have seen cases of gastric ulcer and also cases of gastric carcinoma. The diagnosis of ulcer of the stomach is not always easy; it is made by different persons differently, and their statistics differ. The surgeon with statistics taken from nothing but a surgical practice, or even a surgical hospital practice, will state that carcinoma of the stomach is very frequently encountered, that it is frequently complicated with gastric ulcer, and that there is a frequent connection between the two. He cannot tell you the reality about these statistics, when he forgets or overlooks the fact that they are the bad cases that have disappeared from the hands of the general practitioner to appear in the hospital wards, and that he sees these bad cases only, and not the average ones. The surgeon will report what he has seen, and so far he is correct. On the other hand, the man in private practice who sees the poor patient with ulcer of the stomach will say that ulcer of the stomach is a very common disease, and he will offer quite different and more favorable statistics; he is the one who can tell whether the case has terminated in hemorrhage or in carcinoma. The fact is that from a large number of statistics it has been found that there is about 3 per cent. of the cases of carcinoma occurring in the neighborhood of the pylorus which are on the scar resulting from an old ulcer. I see a great many of these cases of gastric ulcer and especially among the poor, the working people, male and female, small shopkeepers, etc.; these poor people work hard and may suffer weeks and even months before they consult a physician. Many will take care of themselves and they at times will recover in large numbers. We should compare the sources from which these people come to us. The general surgeon, the surgeon in private practice, the physician, the so-called internist, the physician who has a consultant practice only, or a large practice among the rich, the physician who has a large practice among the poor, all these men will give different statistics, and this is a point which we should all be made aware of. The general practitioner has the more correct statistics. I once suggested that 500 general practitioners should club together and all their cases of gastric ulcer with their outcome be collated and compared.

Dr. Harvey G. Beck, Baltimore: If we accept the fact that carcinoma of the stomach results from ulcers, then with a view of preventing the disease, we should consider the origin of the ulcer, and treat the underlying cause. We all recognize that there are different forms of ulcer of the stomach. For instance, we have the chlorotic form which occurs

in girls. If the chlorosis is early diagnosed, and treated, we may prevent ulcers, and indirectly carcinoma. Another form of ulcer is the so-called catarrhal ulcer, which results from a chronic acid gastritis. Here again, if we treat the underlying condition—acid gastritis—we may prevent the ulcer, and the tendency to carcinoma. A third group may be classed as traumatic ulcer. These ulcers are due to an injury or irritation and are frequently the result of occupation. These cases certainly have a greater tendency toward the development of carcinoma, and if they do not yield readily to medical treatment should be treated surgically in order that carcinoma may be prevented.

Dr. G. C. Smith, Boston: During the last 10 years only 2 patients with carcinoma developing on the site of an ulcer of the stomach have appeared in my office. Of the other cases I have had under observation, none has so far developed into cancer. I do not think we are justified in treating these patients along the lines suggested, because there is a possibility of cancer developing on old scar tissue, any more than is the man who treats skin disease who goes on and feels that he must treat the patient indefinitely with mercury. The idea prevails that such a patient has practically recovered from syphilis and that he must be left alone until something develops later, when a short treatment should again be given. I can easily understand the position assumed by Dr. Wilson in his paper. As Dr. Jacobi has so well expressed it, any statistics to be of value depend quite as much on our interpretation of them as upon the mere statement of the anatomic findings. One man has reported many patients with cancer of the stomach operated on, and in many of them he reports that the cancer has developed on an old scar tissue. He is justified in reporting such cases. But he has not seen cases as have Dr. Jacobi, Dr. Stockton, and others, in which the patients were not operated on. Some statistics are given which apply only to those patients who developed cancer; not all individuals, however, develop cancer on scar tissue. It must be remembered that 50 per cent. of patients with tuberculosis recover; this is the report from Prof. Kolisko of Vienna, where it is said that there are more cases of tuberculosis than in any part of the world. But Prof. Kolisko does not state that these patients do not subsequently develop tuberculosis. We cannot state positively that a person has been permanently cured of tuberculosis; we do know, however, that he may become apparently well. This is our interpretation of the facts.

Dr. Frank Smithies, Ann Arbor, Mich.: I wish to act as a sort of mediator between Dr. Stockton and Dr. Hall. There is a middle ground in the consideration of gastric ulcer and gastric cancer, that is, in regard to the prognosis, whether medical or surgical, as well as in the treatment. It depends

to a large extent on the location of the gastric ulcer. I think that it is poor practice to hand these patients over to the surgeon for exploratory operation, or operation of any kind, without having at least made an attempt to determine the position of the ulcer and its effect on the motor power of the stomach. If an ulcer be situated near the pylorus and we have every reason to believe that it has healed, with a resulting scar which produces a certain amount of obstruction to the free emptying of the stomach, I think it is an extremely unwise practice to treat such a patient for a gastric ulcer indefinitely; he is bound to become a chronic dyspeptic when by an operation in the hands of a competent surgeon he can be made a useful citizen and not be left a chronic invalid. Ulcers seem to be very favorably situated for the development of carcinoma when placed where they are constantly subjected to irritation. On the other hand, it is a fault of the internist to recommend operation in all cases of simple ulcer situated in any part of the stomach which has no influence on the stomach so far as its motive power is concerned. Of course in all cases one must make an exact diagnosis. I wish to call attention to the constant and repeated examination of the stools for occult blood, not making a haphazard examination for this occult blood, but making a careful and painstaking examination of the stools that have been properly prepared for such an examination, that is, after an absolutely meat-free diet for at least three days. Another point is to examine the blood serum carefully with the idea of discovering the hemolytic reaction. This is a point which I will not debate at present. However, in carcinoma we may expect positive reaction; whereas in ulcer we do not. Again, one might speak of a very careful examination of the interior of the stomach by means of the gastroscope, but always in the hands of an expert.

Dr. Theodore Potter, Indianapolis: It seems to me that in the discussion so far we are hardly fair to Dr. Wilson. We seem to have engaged in a general quarrel as to the diagnosis and treatment of gastric ulcer, with which he really had nothing to do. He comes to us presenting a careful pathologic study which he hopes may throw some light on the question of the factors which enter into the development of carcinoma. He has shown us that in a considerable proportion of the cases in which the disease has developed, and which have followed ulcer of the stomach, certain things take place and which are very significant. We must recognize them as being significant too. Dr. Wilson has presented studies which certainly will throw some light on this problem as to what is the cause of gastric cancer. With regard to the diagnosis and treatment of ulcer of the stomach, and the question as to what we are going to do about it, this certainly is not Dr. Wilson's affair; that is our quarrel. But please

let us be just to Dr. Wilson and show appreciation for the work that he has done and is doing for us.

Dr. Louis B. Wilson, Rochester, Minn.: No doubt there are cases of cancer of the alimentary canal that have occurred without any previous epithelial segregation. We have one such, a case of carcinoma of the stomach. We have also 5 cases of carcinoma or ulcer of the stomach in which there is a proliferation, or beginning inversion of the epithelium, but I am not prepared to say that they are cases of carcinoma. Every case that I have shown to-day and 183 out of our 189 showed carcinoma in the glands or walls of the stomach. From a pathologic standpoint we are changing our methods of diagnosis. We used to wait until a "lump" was discovered before we diagnosed the case as one of carcinoma of the stomach. This we no longer do. We should not criticize Dr. Hall too severely for his statement that 68 per cent. of the cases resected for ulcer showed cancerous changes. Few known ulcers are excised and there are many in which the surgeon is doubtful as to the diagnosis. The relationship between carcinoma and ulcer so far as we can show is that in many chronic ulcers there is a segregation of epithelium on which carcinoma may develop. Not every person who is exposed to typhoid develops that disease; nor does every person who has been exposed to diphtheria develop diphtheria. The same statement may apply to epithelial segregation. But when we do encounter carcinoma, in the majority of cases there will be found to have been previous epithelial segregation. As to what shall be done with those ulcers, that is for the surgeon, and not for the pathologist, to decide.

THE ELECTROCARDIOGRAM IN CLINICAL DIAGNOSIS

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In the study of cardiac function by instrumental means, a number of methods have been employed, each of which has yielded information which was not obtainable with the others. The study of the arterial pulse has taught us much regarding the relation between cardiac output and peripheral resistance; the study of the blood-pressure has taught us to estimate accurately the force of the heart-beat and the factors which control it; the x-ray examination has given us a means of observing the changes in volume of the four chambers of the heart; and the study of the venous pulse has enabled us to detect many changes in the origin and propagation of the cardiac contraction. In spite of the great additions which these methods have made to the study of the heart, there is still much information that they are unable to furnish, and some of this is yielded by studying the electric variations produced in the body at each beat of the heart.

Considered electrically, the human body may be regarded as a battery with the two arms and two legs as its natural and most convenient poles. Owing to processes going on in the body and in the skin, the potential at each of these poles is different; hence, if any two of these limbs are dipped into zinc pans containing salt solution and connected with one another by wires,

a constant current is generated; and if a very sensitive galvanometer is placed in the circuit it is deflected by this "body current"—or, as it is usually termed, "rest-current."

The rest-current is due simply to the difference of potential between any two parts of the body and is independent of any muscular contraction. Besides this, another current (action-current) is set up whenever any muscle acts, and this action current adds its effect to that of the body current already present and causes the galvanometer to swing each time that it is generated, that is, every time the muscle acts. Action of any muscle can cause such action-currents, and even small movements of the fingers placed in the salt solution are accompanied by very large deflections; but if the patient is kept perfectly quiet and there is no tremor the only important deflections are those caused by the cardiac action.

The electric variations accompanying the cardiac action have an intensity of from 1/1000 to 3/1000 of a volt, and consequently could not be studied accurately until an extremely delicate galvanometer had been invented. Professor Einthoven of Leyden has invented such a galvanometer, which consists of a very fine quartz or platinum thread, so fine that it is barely visible and so light that it can scarcely be weighed by the most delicate balances. This thread is suspended in the field of a permanent magnet or of an electromagnet. When the current from the body passes through the thread, it charges the latter and causes it to be attracted or repelled by the poles of the magnet, and the thread is so light that it is deflected without delay by these changes in the electromagnetic field. The movements of this thread are magnified with a powerful microscope, illuminated with an arc-lamp, and the shadow is photographed on a moving drum 6 or 8 feet away (Fig. 1). By this method, it is possible to study very small currents.

It is even possible to connect distant points with the galvanometer and thus to record the hearts of patients who are lying in their beds in the wards, or to connect the laboratory with distant hospitals; but grounded circuits cannot be used for this purpose. Professor Einthoven has made most of his tracings from patients in Professor Nolan's wards of the Leyden hospital, a mile and a half away from his galvanometer.

Even 1/1000 of a volt is sufficient to cause a marked deflection, 4 mm. with our instrument, 1 cm. with the larger instruments. In Baltimore we have worked with the small permanent magnet and a platinum filament.

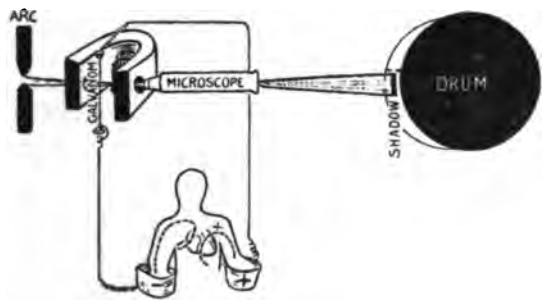

Fig. 1.—Diagram of a simplified electrocardiograph, showing also the distribution of the electrical changes about the heart. The patient is supposed to be seated with his hands immersed in the jars of salt solution (+ and —).

This has given in the main very satisfactory results, but we hope, next year, to have the larger and more delicate apparatus.

The electrical changes during each cardiac cycle are quite characteristic and correspond to the successive activities of the atrium and the ventricle. The base where the atria are situated becomes negative before the atrial activity, which is followed by another, due to the ventricular activity.

As will be noticed, the variations in potential are a little different if they are led off at different parts of the body, and the curves thus derived differ slightly from one another. Since Einthoven's first work, it has

been customary to take records from three different derivations: the right hand and left hand—designated as the first derivation (D1); the right hand and left foot, the second derivation (D2); and the left hand and left foot, third derivation (D3). The second derivation shows the greatest oscillations; the third derivation is the most important for determining hypertrophy of the left ventricle.

The typical form of electrocardiogram is shown in Figure 2. As can be seen, the first wave (P) is a small one due to activity of the atria (P wave). This is followed by a very small depression of the curve below the base line, Q depression. Then comes the wave due

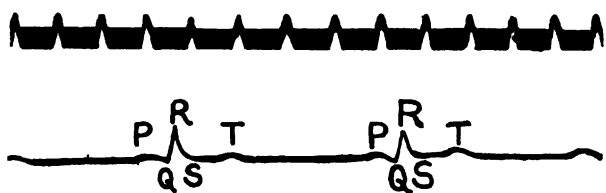

Fig. 2.—Typical electrocardiogram from a normal man. Current led off from right hand and left foot (D 2). Upper line, timer marking fifths of seconds.

to the action of the ventricles, a large wave (R), which sets in suddenly and as suddenly subsides, falling below the base line (S depression), and this wave in turn is followed by a small second wave (T) which occurs during the middle of systole (Fig. 3).

The most recent investigations of Kahn in Hering's laboratory indicate that the electrical variations and the mechanical action are synchronous, and that the electrical variations do not precede the contractions as was first supposed, although the former slightly precede the rises in intra-atrial and intra-ventricular pressures. We have, however, used the term "activity," rather than contraction in the above descriptions, as this leaves the matter open pending confirmation of Kahn's work.

The mode of origin of the T wave is more obscure, as there is no separate contraction which corresponds to it, but the two ventricular waves (R and T) correspond closely to the first and second waves of the diphasic variation which is seen in the contraction of any muscle whatever. Moreover, the form of the electrical curve is scarcely due to the algebraic sum of the curves of the two ventricular contractions, as claimed by Kraus and Nikolai, since the same curve was obtained by San-

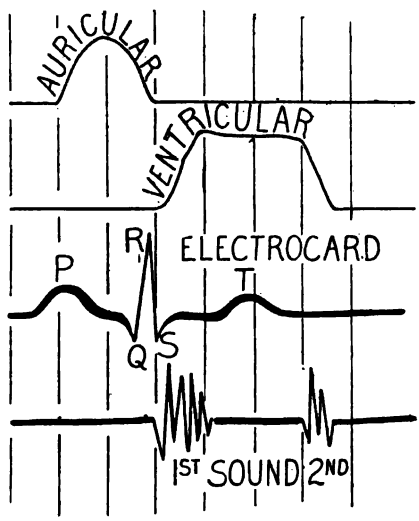

Fig. 3.—Diagram showing the time relations between the waves of the electrocardiogram, the heart sounds and the contractions of auricles and ventricles.[1] Vertical divisions indicate tenths of a second.

derson and Page and, more recently, by Gotch in the frog and tortoise, although these animals have only one ventricle (Fig. 3.)

So much for the normal electrocardiogram. When the left ventricle is hypertrophied, the electrocardiogram undergoes a very definite change, and the first ventri-

1. The short interval between the beginning of the R wave and the beginning of the rise in intraventricular pressure is interpreted by Kahn as due to the phenomena of conduction within the heart. In experimental ventricular extrasystoles the electric and mechanical changes are absolutely synchronous.

cular wave (R) becomes inverted (Fig. 4). Occasionally the T wave is inverted also.

The electrocardiogram is also particularly useful in the diagnosis of heart-block. Figure 5A shows a venous

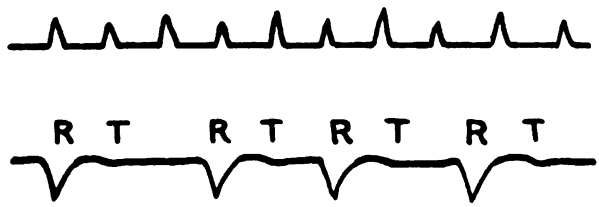

Fig. 4.—Upper line, timer, marking fifths of seconds; lower line, electrocardiogram. Inversion of the R and T waves due to hypertrophy of the left ventricle. Current led off from left hand and left foot (D 3). The P. wave due to the atrial activity is absent.

and arterial tracing from a case of permanent, complete heart-block with the auricular rate about twice the ventricular. Figure 5B is an electrocardiogram of the same

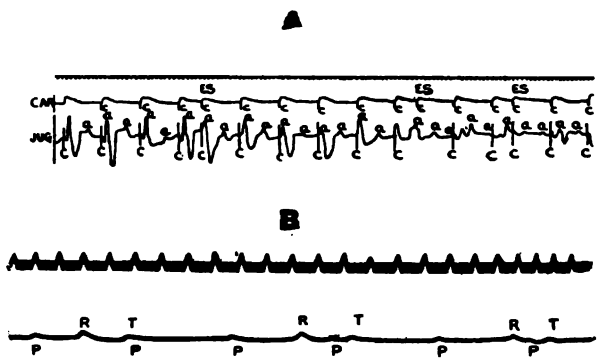

Fig. 5.—A, Venous and carotid arterial pulse from a patient with complete heart-block and pulse-rate of 33 per minute. B, electrocardiogram from the same patient. Upper line, timer in fifths of seconds, lower line, electrocardiogram. The rate of the atria is about twice that of the ventricles but the complete dissociation between the two is more readily discernible in the electrocardiogram than in the venous tracing.

case, in which, as will be seen, the complete dissociation is much more easily made out.

One of the most interesting variations is that which is obtained from the extrasystoles, as is seen in Figure 6.

It will be noticed that the wave accompanying the extrasystole is unusually large and slow. It is so different from the normal beats which precede and follow it that one can tell by merely watching the string just when an extrasystole takes place. It will be noticed that the first wave is very large, that it subsides very slowly and is

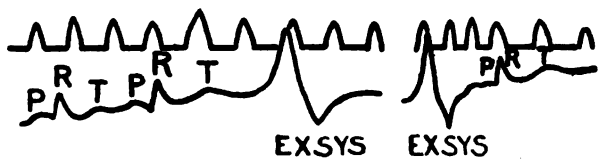

Fig. 6.—Electrocardiogram showing extrasystoles which probably arise in the right ventricle. Upper and lower lines as before.

followed by a very large depression (Fig. 6). Kraus and Nikolai have shown that this type of curve is given by extrasystoles which arise in the right ventricle, whereas if the extrasystole arises in the left ventricle one obtains the exact inverse of this curve (Fig. 7). Recent investigations by Kahn have shown that stimuli which arise near the apex give about the same form of curve in either ventricle, in whichever ventricle they may arise. These types are not absolutely distinctive.

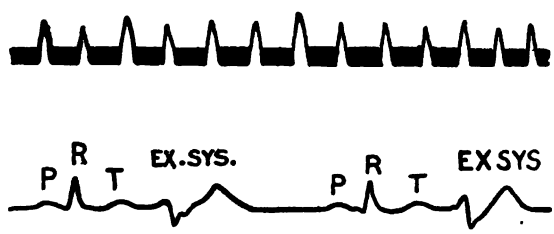

Fig. 7.—Electrocardiogram showing extrasystoles which probably arise in the left ventricle. Upper and lower lines as before.

If the extrasystole arises in the atria, the curve is preceded by a P wave, and it often resembles the normal electrocardiogram much more closely.

Occasionally one encounters cases in which the P wave due to the atrial activity has disappeared, and is replaced by irregular waves of a frequency varying from

300 to 900 beats per minute (Fig. 8). As Rothberger and Winterberg and, more recently, T. Lewis have shown, this form of curve is associated with fibrillary contractions of the atria, and is especially frequent in the permanent, absolute arrhythmia. This curve is obtained most frequently when the current is led off from the third right interpace and left interscapular regions—that is, when the circuit passes through both atria. Our own curve is obtained from the second derivation in the same patient as the left-sided ventricular extrasystoles, a patient with paroxysmal tachycardia between attacks.

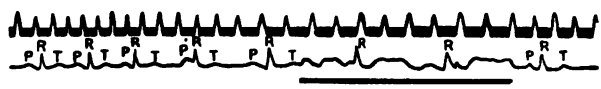

Fig. 8.—Electrocardiogram showing fibrillation of the auricles in the portion underlined. Upper and lower curves as before.

Evidences of atrial fibrillation cannot be obtained with venous pulse, as the fibrillating auricle does not give any wave on it; and so the only evidences of this state can be revealed by the electrocardiogram. The studies of Cushny and Edmunds, of Hirschfelder, of Rothberger and Winterberg, and of Thomas Lewis indicate that this may open up an entirely new field in our knowledge of the permanent irregularities of the heart and of paroxysmal tachycardia, and in the study of many functional disturbances which are at present quite mysterious.

It seems probable, therefore, that this new method will enable us to penetrate one step further into the problems which cannot be solved by the older procedures, and will bring us closer to a perfect understanding of what goes on in the diseased heart.

It is also possible to obtain graphic records of the heart-sounds by means of Einthoven's galvanometer. This procedure has nothing to do with the electrocardiogram and there is no direct connection between the

galvanometer and the patient's body. The galvanometer is merely connected in circuit with the secondary coil of a very delicate telephone, or rather a microphone so that it takes the place of the telephone receiver.

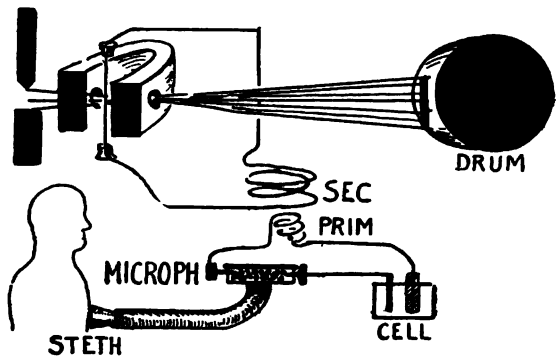

Fig. 9.—Scheme of simplified arrangement for the recording of the heart sounds. *Steth*, stethoscope; *Microph*, microphone; *Prim*, primary coil; *Sec*, secondary coil.

A stethoscope is held on the patient's chest and the heart-sounds are led to the microphone through a rubber tube. The sound waves cause telephone currents

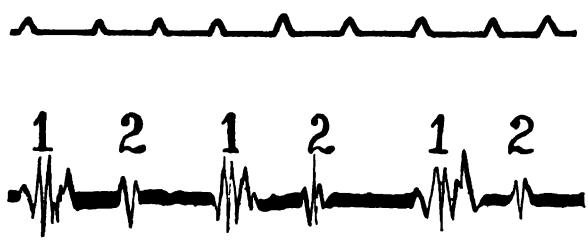

Fig. 10.—Graphic records of the heart sounds from a normal individual. Upper line, timer in fifths of seconds; lower line, phonogram.

which are transmitted to the galvanometer and cause the string to vibrate. The vibrations of the string are photographed and graphic records of the heart-sounds are thus obtained (Fig. 9).

Figure 10 shows such records of normal heart sounds. It will be noticed that vibrations of the first sound last

only about 8/100 to 1/10 second. The short pause is about 15/100 to 25/10 and the second sound lasts 5/100 to 8/100; while there is a long pause in diastole.

Figure 11 shows a record from a little girl with a presystolic rumble and a systolic murmur at the apex.

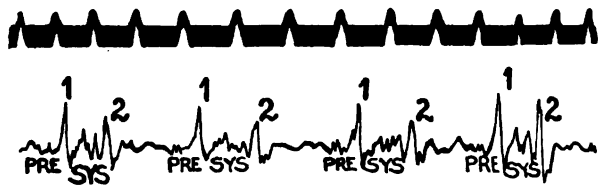

Fig. 11.—Graphic record of heart sounds from a patient with mitral stenosis and insufficiency. *Pre*, presystolic rumble; *Sys*, systolic murmur. Upper and lower lines as in Figure 10.

The small vibrations correspond to the rumble just before the first sound, and the large vibrations correspond to the heart sounds.

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ABSTRACT OF DISCUSSION

Dr. J. A. Lichty, Pittsburg, Pa.: I should like some information regarding the lettering of these waves; have the letters used any significance? I should like to know more, too, regarding the A-wave in particular; the A-wave is always mentioned and looked for, and I should like to know if the lettering of the A-wave is an arbitrary lettering, or if it possesses some special significance.

Dr. John H. Musser, Philadelphia: I should like to call attention to the importance of all these studies, not only the studies with the apparatus which has just been presented, but also the studies with the ordinary Jacquet instrument by which it is made possible to differentiate the various myogenic functions of the heart. This is very important in diagnosis and prognosis. It has also occurred to me that we can draw excellent conclusions as to methods of treatment. When we find in one man that there is an excess of stimulus production or of excitability, a depression of conductivity or contractility or a loss of tonicity, when coupled with certain blood-pressure changes, we have a guide at once for methods of treatment that is not based on empirical grounds, but is actually scientific. In the discussion on the question of heart failure and the reports of the various investigations concerning it, I had in mind to call attention to the value of mor-

phin as a remedy in the earlier periods of heart failure, for two reasons. First, we realize, of course, that in the prevention of heart failure we should take into consideration the fact that there is a failure as well occurring in other portions of the organism, and particularly the nervous system. One of the first indications of heart failure perhaps is undue excitability or excess of stimulus production. Second, there is the immediate action of morphin on the heart. If we can uplift the condition of the nervous system, or reduce its wear and tear, both of which may be factors in the production of cardiac failure, by the use of a remedy such as morphin, we are going a long way in the prevention of cardiac exhaustion. I think therefore that morphin is a valuable aid directly and indirectly: directly by its action in lessening excitability or perhaps stimulus production; indirectly, through the nervous system. Other remedies or measures may be employed to control these disturbed myogenic functions. Furthermore, when we find that there is depression of conductivity, the remedy to be employed—atropin or belladonna—and other remedies come to our minds at once. For the depression of contractility the nitrites, among many other remedies, are necessary, and in loss of tonicity, digitalis and other heart tonics are of avail. In differentiating the remedies required, the degree of tension of the vessels is a valuable aid. I have been at sea recently and frequently in regard to the employment of remedies for the complicating conditions present in cardiac exhaustion. I have had great satisfaction resulting from studies such as these in determining the lines of treatment, and for this reason I wish to call attention to the importance of observations which help us in this matter.

Dr. Richard Weil, New York: I think it would be of interest to analyze the evidence offered by this new method with reference to the question of nodal rhythm. It seems impossible to determine definitely by the older sphygmographic method whether the coincidence of the jugular and the radial impulses was due to synchronous contractions of the auricle and ventricle—the nodal rhythm theory—or whether it was due simply to the propagation of the systolic ventricular impulse through the paralyzed auricle into the jugular. I should like to know whether the galvanometer method has in such cases determined the presence or absence of a true auricular contraction.

Dr. A. D. Hirschfelder, Baltimore: The A-wave is so-called because the wave is caused by the auricular contraction. The letters P, Q, R, S and T of the electrocardiogram are purely arbitrary, but the P-wave is probably so named because it is a presystolic wave. I know of no significance of the lettering of the other waves, except possibly the letters of the alphabet following the P were used for the sake of convenience. P was selected first because it was the first letter of presystolic.

I agree with Dr. Musser that the most important thing for us at present is carefully and with accuracy to analyze the possible effects drugs are having or are producing, studying the maximal and the minimal blood-pressures, the venous pressures, the electrocardiograms, and also any changes in the cardiac outline. We should study the changes in force and the venous blood-pressure, the tendencies to overfilling of the heart, the changes in the tonus of the heart muscle, (i. e., the tendency of the heart to resist overfilling) and we should study as well the electrical changes which accompany changes in the cardiac impulses.

Many of the venous tracings, especially those having to do with the wave due to synchronous contraction of the auricle and ventricle, admit of doubtful interpretation. Some of the waves which appear during ventricular systole coincide with the C-wave and appear to be due to a fling of the lever. The electrocardiograms taken so far have not shown any evidences of nodal rhythm. Experiments with animals show simultaneous contractions of auricle and ventricle. On the frog's heart we can show contractions of the muscle ring that corresponds to the His bundle. The muscle ring can be seen contracting. When an abnormal stimulus acts first on this ring it contracts first and the auricular and ventricular contractions follow directly the contraction of the ring. The auricle and ventricle then contract simultaneously. However, this does not prove that a similar phenomenon occurs in all the cases which MacKenzie has ascribed to it in man. This whole subject is a matter for further careful investigation.

PERSISTENT PATENCY OF THE DUCTUS ARTERIOSUS

DEGENERATION OF THE CARDIAC MUSCLE AND CORONARY ARTERIES, AND OF THE SINO-AURICULAR BUNDLE, FOLLOWED BY RUPTURE OF THE RIGHT VENTRICLE

KATE CAMPBELL MEAD, M.D.,
MIDDLETOWN, CONN.

One of the most interesting problems of physiologists to-day is concerned with the structure and action of the heart. So much experimental work has been done during the past few years on the cardiac muscle, nerves, valves, and blood supply, as well as on the arterial system, by means of measuring apparatus and surgical operations, that any extraordinary case of heart failure which can be studied during life and post-mortem should be made available for future reference, as an addition to our sum-total of knowledge of congenital anomalies, as well as of inflammatory disease.

It is for this reason that I have ventured to make a slight contribution to the literature on congenital cardiac malformation, which in this case was associated with a sequence of disorders of the heart and its valves, resulting in a rare condition of rupture of the right ventricle, and in the death of the patient at the age of 26.

In presenting this report I must express my regret that no sphygmographic tracings or electrocardiograms were made from the heart, the arteries, or the veins; but a brief study of the conditions as a whole may not be unprofitable, although a full discussion of such a case would far exceed the limits of this paper.

REPORT OF CASE

History—The patient was a married woman. Of her early history there is little known; she told me she had always had rheumatism and backache, had suffered frequently from grip, and that her physicians in Berlin, Germany, said she had heart trouble since she was a little girl. Her parents and grandparents were healthy. I first saw her April 3, 1905, and her condition was as follows: Height, about 5 feet, 4 inches; weight, 120 pounds; body, plump; color, good; some acne on face; catarrh of throat and nose; lateral and anterio-posterior curvatures of the spine due to muscular weakness, simulating both scoliosis and kyphosis; aortic pulsation in the abdomen noticeable; heart enlarged 1 cm. to right and left, with a murmuring, noisy systolic murmur heard both at base and apex, extending to right of the sternum and almost to the axilla; lungs normal; bowels distended with gas; diarrheal movements; stomach larger than normal; liver normal; left kidney in left groin; pelvic organs normal; urine normal.

After a summer of rest and hygienic life the cardiac murmurs nearly disappeared, but the patient continued to suffer from backache, diarrhea, and catarrh of the throat. The following year she went through a successful pregnancy in better health than usual, even omitting colds and grip. During the summer of 1907 she had a nervous strain which was followed in the early autumn by a condition of flabby muscles and flabby heart, with loud systolic murmur over the pulmonary artery in the third space, and a strong thrill felt over the third and fourth interspaces at the right of the sternum, and frequent palpitations. Her intestinal indigestion was very troublesome, and the facial acne most annoying. Hygienic treatment, baths, massage, careful diet, and occasional doses of codein gave considerable relief, while digitalis, even in minute doses, caused most uncomfortable bounding and beating of the arteries all over the body.

At the end of December, 1907, I referred the patient to Dr. Thayer of Baltimore, who sent me the following diagnosis:

"There is evidently a congenital malformation, but one which from her history and condition, may well be compatible with a long life. The long machinery murmur over the right ventricle with systolic accentuation, together with the accentuation of the second pulmonic sound, and the rather large right side suggest a septum defect (ventricular). This lesion is also more compatible with long life than most other cardiac defects. A striking feature of this case is the fact that the murmur is so loud at the base and in the first left interspace, and that the accentuation high up is late, a late systolic, almost a diastolic

accentuation, but the murmur still continues throughout both cycles of the heart with the heart sounds heard, as it were, superimposed. The loudness of the murmur high up and the change in its accentuation would suggest to me an open ductus arteriosus." [1]

During 1908 the patient was fairly well so long as she lived a quiet life and refrained from lifting heavy objects, which gave her pain in the abdomen and slight palpitation of the heart. In November she suffered from another attack of influenza, with tonsillitis, slight bronchitis, and a little pleurisy at the base of the left lung. The mild fever left her very much exhausted, with a hoarse voice and irritating cough, due apparently to a large lingual tonsil and relaxed uvula, but with no new cardiac symptoms, either objective or subjective. She continued hoarse, and although the cough was gone by the end of February, 1909, her heart began to be more dilated and to have the murmurs and irregularity first heard in 1906. After a visit to Lakewood, in April, however, she gained several pounds in weight and felt better, although there was now in addition to the hoarseness a peculiar thin voice.

On April 22, 1909, I referred the patient to Dr. E. Terry Smith of Hartford, who reported a paralysis of the left vocal cord, caused probably by pressure from the heart on the abductor fibers of the left recurrent laryngeal nerve.

A report by Dr. Goodale of Boston, a week later, confirming Dr. Smith's diagnosis, was as follows:

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1. I have taken the following notes from Dr. Thayer's memoranda: "Weight, 121½. Color is good. General nourishment good. Pulse, 21 to the quarter at the beginning of examination, regular. Radial, not palpable. Pressure, by estimate, 120-25; measurement, maximum, about 115; minimum not easy to estimate. Thorax, symmetrical. Costal angle about 90. Movements, equal. Resonance and respiration clear in front. Back perfectly clear. Heart, P. M. I. in the fifth space, approximately normal position, 8.6 cm. from the median line, begins above in the second space and extends about 5.5 cm. to the right of the median line in the fourth space. No thrill in the precordial region, although the impulse is rather well felt in the second and third left spaces. Sounds, at the apex, first clear excepting for a soft systolic gradually fading away. Second, clear, followed by a very soft diastolic. As one reaches the fourth space a characteristic long machinery sound with systolic accentuation lasting through the whole cycle is audible. This is loudest in the third space, well heard in the second, also over the right side and out over the left chest. In the first left space under the clavicle the murmur was also very long and well heard with late systolic or, perhaps, even diastolic accentuation. The second pulmonic is loud and sharp. The second aortic is also of fairly good intensity. Right kidney descends below the costal margin. Liver is just felt descending below the costal margin on deep inspiration; no enlargement. From the character and position of the murmur one is justified in assuming a septum defect, and from the murmur which is heard up under the clavicle in so high a position, an open ductus Botalli."

"April 30, 1909. Left vocal cord fixed in median line, immovable on phonation and respiration. Left arytenoid moves inward slightly on phonation. There is no evidence of thickening or irregularity in or about the arytenoids.

"The preservation of motion in the left arytenoid on phonation is due to the contraction of the interarytenoid muscle, indicating preservation of function in the superior laryngeal nerve. This movement, together with the absence of irregularity or thickening in the left arytenoid joint, renders it probable that there is no ankylosis in the joint itself. It is, of course, possible that Mrs. X.'s abductor paralysis arises from grip or laryngitis, but this is, to my mind, less probable than that it arises from pressure along the course of the nerve, for the reason that general infections do not, as a rule, affect the abductor fibers alone of one cord."

The patient was then sent to Dr. Percy Brown of Boston, who made a Roentgen diagnosis of her heart as follows:

"The base of the heart, examined from both behind and in front, presents an undue and abnormal bulging on its left side, which markedly changes the shadow usually recognized as the normal in form and size. This appearance is in close juxtaposition with the descending arch of the aorta, and may to a certain extent involve that structure. The dilatation is general, however, rather than a sharply localized expansion, which would tend to rule out the likelihood of aneurism as being the etiologic factor. I am rather of the opinion that it is due to a hypertrophied and dilated left auricle, secondary to an insufficient mitral valve. This dilatation is the only apparent cause of the mechanical inference with the function of the recurrent laryngeal branch."

For one month, while the patient was living quietly and taking simple vocal lessons, the heart symptoms again improved and the voice became nearly normal, but on June 1 she complained, when walking, of severe paroxysmal pains in the abdomen and legs, especially in climbing stairs or going up hill. The heart was not then larger than usual and the murmurs were faint; pulse 80; systolic blood-pressure was 118, and hemoglobin normal; urine normal. On June 5 the apical mitral murmur of 1906 returned, and the left area of dulness extended 3 cm. to the left of the nipple; pulse 100. On June 11 the pulse was 70 and regular, but a hard, suffocating pain was centered in the stomach and abdomen, at times accompanied, when walking was attempted, by severe pressure below the diaphragm. This persisted for one week, when some edema was noticed in the face and abdomen; the patient passed 500 c.c. of urine in eighteen hours full of urates, but

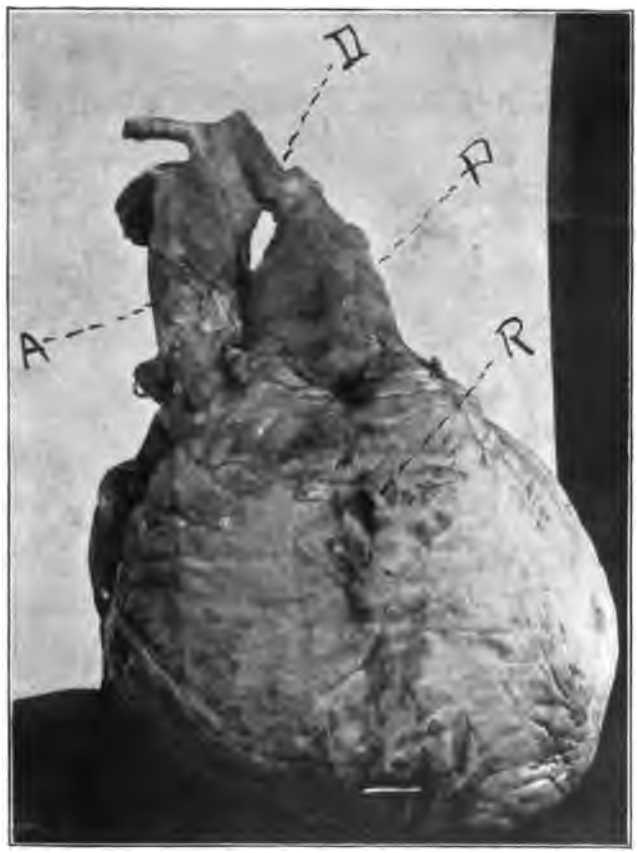

Fig. 1.—Heart from subject with persistent patent ductus arteriosus; A, aorta; D, ductus arteriosus; P, pulmonary artery; R, ruptured right ventricle.

Fig. 2.—Rupture seen from apex of heart.

containing no albumin, the specific gravity being 1040; her radial blood-pressure was 140. Digitalis being contraindicated, warm Nauheim baths were given, plus strophanthus and diuretin; the urine increased to 900 c.c. for a few days and the abdominal girth was reduced 6 cm.; at the same time the heart sounded stronger, and the edema left the face. Then, however, the stomach became irritable, the heart began to be very irregular with loud aortic murmur, and all baths and heart tonics were replaced by calomel, Epsom salt, and codein. On July 5, the voice again showed signs of the former paralysis, and a laryngeal cough was almost constant; the pulse was 105, pressure 130; the legs were very much swollen; the stomach and bowels were full of gas and the urine scanty.

On July 9 she could not rest for a moment, owing to the laryngeal cough and cardiac discomfort; at 5 a. m. of the 10th she broke into a profuse cold perspiration; at 7 a. m. she seemed faint and lapsed into a short stupor, after which until death no pulse could be detected at the wrist, even though hypodermic stimulants were freely injected; the carotid pulse was 104, very irregular, and the patient had difficulty in breathing, was restless and thirsty all day, dozing at brief intervals; she took a little nourishment and passed about 7 ounces of thick urine. At 10 p. m. she had another period of fainting with profuse perspiration and gasping, after which she could with difficulty be aroused, her speech was somewhat incoherent and thick, and she was still very restless. At 12:55 a. m., after swallowing a few drops of liquid, she suddenly threw up her arms, opened her eyes widely, gasped once or twice, and died.

So much for the patient's symptoms while under my care. Her earlier medical history is very meager. She was born in Berlin, Germany, a perfectly normal birth and a typically healthy baby, it was thought, but the physicians of her childhood are dead. A letter from Dr. Max Ph. Meyer, Geh.-Sanitätsrath, gave the following information: There was a systolic murmur over the mitral valve, which was louder during the fever of measles in 1895. In 1899, after a period of fatigue, the aortic valves were not found to be free from chronic inflammation, the tones not being quite clear. A note from Dr. Geheimrath Wolf says: "After two examinations, I found a good compensation in the heart (ein gut compensierter Herzfehler)."

Owing to the peculiarity of the symptoms in this case and the lack of early history, together with her early death, it

seemed wise to seek for a postmortem diagnosis in order to make it possible to use for future cases whatever could be learned of the exact causes for the cardiac weakness in this patient. Dr. Jessie W. Fisher, pathologist to the State Asylum for the Insane at Middletown, Conn., performed an autopsy with the following result:

"*Autopsy.*—Some twelve hours post-mortem. Rigor mortis moderate. The patient was a well-developed, well-nourished, but undersized woman, 26 years of age, with distended abdomen, edematous feet and legs, and cyanosed face and neck. Panniculus adiposus was 3 cm. in thickness. The stomach was much distended with gas, and the abdominal cavity contained at least 2,000 c.c. of straw-colored fluid.

"Thorax: Both parietal and visceral layers of the left pleura were adherent laterally, posteriorly, and to the diaphragm. The right pleura was free.

Left Lung: "Weight was not taken. The lower lobe showed hypostatic congestion, the remainder of the lung being crepitant, presenting no abnormalities. Bronchi free and unobstructed.

Right Lung: "Lower lobe showed a slight amount of hypostatic congestion. Otherwise the tissue was normal.

Heart: "The pericardium was smooth and glistening and covered by a very thin layer of fat. The pericardial sac contained about two ounces of fluid blood. When the sac was opened, three ruptures on the right ventricle appeared, parallel to the descending branch of the anterior coronary artery, and 3 cm. to 4 cm. to the right of it. The first was 2.5 cm. from the pulmonary valve, and was 9 mm. in length, slit-like in appearance, involving only the superficial fibers. The second was near the apex of the heart and measured 15 mm. in length externally and penetrated the ventricle by a minute aperture. The third, immediately below and on the apex of the right ventricle, was 15 mm. in length externally, but presented only a pin-point opening internally.

"At autopsy the ruptures seemed to be in the left coronary artery, but on later dissection of epicardial fat the first rupture lay 3 cm. to the right, and the second and third ruptures 4 cm. to the right of the left coronary.

"The ruptures lay in almost a straight line with each other, and the blood had separated the epicardium above and below them, giving the appearance of a thrombosed vessel.

"The ductus arteriosus was patent and had developed into a good-sized vessel, with walls 1.5 mm. in thickness. The diameter of the opening into the aorta was 1 cm., and into

the pulmonary artery was 4 mm., where it was surrounded by a thickened ring, and slight fold of membrane. It was funnel-shaped with large end in aorta and 1 cm. in length. The aortic opening of the duct was located opposite the left subclavian artery.

"Heart weighed 395 gm. (Osler gives the weight of a normal female heart as 250 gm.)

"The heart was in systole. The right side was dilated and hypertrophied, containing fluid blood. The right auricle and ventricle were nearly twice as large as normal, and the right ventricular wall was almost as thick as the left, which was also hypertrophied. The foramen ovale was closed, but the fossa was 2.5 by 1.5 cm. At its base the Eustachian valve formed a membranous valve 1.5 cm. in width and 4.5 cm. long, containing muscle fibers.

"Beneath the epicardium of right ventricle there was a marked accumulation of fat, which covered the myocardium and coronary arteries completely.

"The myocardium was thickened, pale in color, and flabby, especially in the right ventricle.

"The auriculoventricular node was well marked, lying between the fossa ovalis and enlarged Eustachian valve. The fibers seemed to pass to the left, where they were lost.

"The ventricular septum was thickened without any indications of defect.[2]

"The pulmonary artery was almost twice the size of the aorta; it was soft, and the aorta slightly thickened around the duct and valve. Insertion of the duct into the aorta was almost at a right angle.

"The cusps of the pulmonary valve were smooth, thin, transparent and competent. The cusps of the tricuspid valve were smooth, glistening and competent. The aortic cusps were slightly thickened throughout and the aortic opening stenosed. The aorta showed plaques of sclerosis around the valve. The cusps of the mitral valve showed slight thickening along the free borders. This opening was small and stenosed. The descending branch of the left coronary was small and walls thickened, but not calcareous. The right coronary was larger than the left, and like it thickened throughout its course.

"Measurements: Tricuspid, 11.5 cm.; mitral, 8.5 cm.; pulmonary, 7.0 cm.; aortic, 5.0 cm.; left ventricle, 1.3 cm.; right ventricle, 1.1 cm.

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2. The thickness of right ventricle wall is normally 4-7 mm.; left ventricle, 20-25 mm.; left auricle, 3 mm.; right auricle, 2 mm.

Larynx and Trachea: "The recurrent laryngeal nerve was normal in appearance, as was the vagus. The larynx, vocal cords and trachea presented no evidence of pathologic change, except for a small tracheocele situated just above the bifurcation of the trachea. Microscopically, the recurrent laryngeal nerve showed no degeneration with Marchi's stain.

"Microscopic examination of muscle near site of rupture: eosin and methylene blue sections stained poorly, nuclear outline faint or nuclei entirely absent. Muscle fibers separated from each other, and intervals filled with red blood cells. Cross striations very distinct. Some fragmentation. Soudan III sections showed muscle cells loaded with fine granules of fat. Hematoxylon and eosin same as methylene blue and eosin.

"Kidneys: The kidneys were pale in color. The capsule peeled easily, leaving a smooth surface. On section the tissue was pale; the cortex was a trifle narrower than usual, but the markings were distinct. On microscopic examination of the kidneys, capsule of Bowman showed considerable thickening and swelling of the cells lining the capsule, and the epithelial cells lining the tubules were swollen and granular. All of the vessel walls showed extreme thickening.

"Liver: The liver was slightly enlarged, but was not removed for examination.

Anatomic Diagnosis.—"Rupture of the heart and sclerosis of coronaries, patent ductus arteriosus, aortic and mitral stenosis and chronic endocarditis of aortic and mitral valves, atheroma of aorta, hypertrophy and dilatation of right heart, tracheocele, slight chronic nephritis, fatty degeneration of myocardium."

Having the autopsy report, it was not difficult to explain the symptoms during the life of the patient, for, doubtless, the primary cause of all the pathologic findings in this heart was the persistent patency of the ductus arteriosus. Dr. H. Gideon Wells[3] has found in all literature only forty-one cases of uncomplicated ductus arteriosus reported with corroboration of the diagnosis at autopsy, and in only twenty of these cases did the subject reach maturity.

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3. Wells, H. Gideon: Persistent Patency of the Ductus Arteriosus, Am. Jour. Med. Sc., 1908.

In Maude E. Abbott's[4] tabulated series of 19 cases of patent ductus arteriosus, the oldest patient was 53, the youngest 6 years old; nine were males, ten females. Out of 106 cases of patent ductus arteriosus, there were eighty-seven cases complicating the defects, leaving the above-mentioned nineteen cases which were proved at autopsy to have the simple defect of patent ductus arteriosus. She gives as causes for this defect the loose musculature of the artery, the sudden change in cardiac blood-pressure at birth, and the alterations in relative position of the ductus and great vessels due to stretching, etc. The usual funnel shape of the ductus is caused by the back pressure of blood from the aorta into the pulmonary vein, but where there is congenital aortic stenosis the current should be reversed. The pulmonary artery and the right ventricle must naturally dilate, and arteriosclerotic patches are not uncommon in the neighborhood of the patent duct and aorta. As for symptoms of a patent ductus arteriosus there may or may not be a systolic thrill, but the "long machinery murmur" is nearly always produced, and the accentuated second pulmonary sound distinguishes this anomaly from pulmonary stenosis. Several other writers have also mentioned the paralysis of the left recurrent laryngeal nerve, due to pressure on that nerve by the patent duct or enlarged auricle, which causes a laryngeal spasm prolonged for hours at a time, giving the right ventricle no time to recover from the added resistance to its contraction, and therefore aiding permanent dilatation of the right side of the heart with all its attendant evils.

My case differed in many points as to symptoms from that reported by Dr. H. Gideon Wells. His patient was 42 years old, suffered from symptoms of gall-duct disease or of acute yellow atrophy of the liver, and died from a hemorrhage of the bowels with a temperature of

4. Abbott, Maude E.: Statistics of Congenital Cardiac Disease (400 cases analyzed), Osler's Modern Medicine, iv, 396.

106, after a few days in the hospital. The previous history of his case was negative, and the examination of the heart when the patient entered the hospital showed systolic murmurs from the second to the sixth right interspace, so that a tentative diagnosis was made of aortic dilatation with enlarged heart. In the case of my patient, there was no other disease of the body and no symptoms not explained by the condition of the heart, which, however, was well hypertrophied and did not appear by percussion or palpation or ausculation to be unequal to its task. This patient was very susceptible to influenza, having one or two attacks every year. These attacks always increased temporarily the cardiac irritation, and the murmur was at such times much more noticeable than at other times.[5] In 1906, when the patient went through a successful pregnancy, the murmurs were very slight, not recurring until after a nervous strain six months later.[6]

It is probable that our patient might have had no symptoms from the large patent ductus arteriosus if she had had no influenza and no other subsequent cardiac complications. Death from a patent duct is usually thought to occur in infancy, although the condition is one which might be overlooked in autopsy, and 9 out of 41 patients whose cases are reported by Wells lived more than forty years.

The characteristic signs of patent ductus arteriosus are in the main those indicated by Dr. Thayer after examining our patient. Osler's[7] terse symptomatology of a persistent ductus Botalli is as follows: "Loud, especially vibratory, systolic murmurs, with the point of maximum intensity over the upper third of the sternum,

5. Schlagenhaufer's case of acute aortic endocarditis from the influenza bacillus in a case of patent ductus arteriosus suggests, along with my case, the possibility of the infection from influenza being more virulent than in ordinary cases.

6. One such case is reported in which the diagnosis of patent ductus arteriosus was made in infancy, and again ten years later, and also at the age of twenty years, when Balfour confirmed the diagnosis, after which time the condition began to disappear until, at the age of thirty-five the lesion seemed to have healed entirely.

7. Osler, William: Practice of Medicine, p. 769.

associated with a lack of marked symptoms of hypertrophy of the left ventricle." Thayer suspected also a septum defect on account of the character of the murmur over the third and fourth space, but this defect was not found on autopsy. Communication between the aorta and pulmonary artery might cause much the same symptoms as from the communication between the auricles. Their etiology is different, but the physical signs of hypertrophy with systolic murmurs at apex, and generally a diastolic murmur, or continuous murmurs[8] are common to both conditions. A septum defect is, however, frequently found in hearts in which there is also patent ductus arteriosus. W. Langdon Brown[9] says: "The deficiency in the exit of blood from the right ventricle will be made good to some extent by the ductus arteriosus remaining open."

Studies in embryology teach us the function of the ductus arteriosus in the fetus: During prenatal life the placental circulation is most important, and the fresh blood must be short-circuited to the brain by being sent through the foramen ovale from the right to the left auricle, thence to the brain, from which it returns to the right auricle again. Here its current is prevented by the Eustachian valve from mixing with the placental stream, and it is sent partly to the lungs, which need very little blood, but mainly through the ductus arteriosus to the descending aorta. When the infant takes its first breath, the lungs expand, causing a fall of pressure in the right auricle and a rise in the left auricle, thereby closing the foramen ovale forever, and at the same time the aorta, which now bulges with blood, is so pressed against the ductus arteriosus as to block the flow of blood through it. But if the natural conditions are interferred with, both the foramen ovale and the ductus are liable to remain open. If, besides this, there is any stenosis of the aorta, there follows an

8. Osler, W.: Practice of Medicine, p. 367.
9. Brown, W. Langdon: Physiological Principles in Treatment, p. 308.

obstruction to the complete emptying of the right ventricle because the arterial blood presses back into the pulmonaries, and the right ventricle becomes dilated and hypertrophied. At the same time the left auricle is dilated and the left ventricle hypertrophied in order to keep up the proper pressure in the stenosed aorta. The right ventricle in the case I am discussing was nearly twice as large as normal, and as thick as the left ventricle. The pulmonary artery was necessarily dilated almost twice the size of the aorta. The ductus arteriosus was so large as to press on the left recurrent laryngeal nerve, although the dilated right auricle may have contributed to the pressure and consequent paralysis of this nerve, which was relieved for a few weeks after the patient began the massage and rest-cure.

It is possible that a ductus arteriosus once closed may reopen soon after birth, owing to a bronchitis or to pleural effusions which raise the pressure in the pulmonary veins, and a permanent aneurism or a permanently open canal may be the result, instead of the usual sclerotic withering down to a fibrous cord. The length of the duct varies from 20 mm. to nothing. The diameter of the lumen is 3-6 mm. up to 1 cm. or more. Sanders in 1860 described one which would admit his little finger. In my case the duct opened into the aorta by an aperture of 1 cm. and into the pulmonary artery by an opening of 4 mm.

Let us now look at the patient's subjective symptoms, as explained by the condition of the heart at the autopsy, and then at the objective symptoms which called forth various hypotheses.

The patient's early symptoms had been those of rheumatic back and throat, intestinal indigestion, and facial acne. There was a flabbiness in the muscles of the back resembling scoliosis, and a relaxation of the tissues in the throat with chronic catarrh. In the abdomen a large round body could often be felt in the left groin, and sometimes also in the right, which seemed to be a

Fig. 3.—A, aorta; P, pulmonary artery; D, ductus arteriosus laid open, showing the opening into both the aorta and pulmonary artery.

Fig. 4.—Radiograph taken three months before the death of the patient by Dr. Percy Brown, Boston.

kidney and which was easily replaced, with relief of the intestinal symptoms. At the autopsy both kidneys were found to be firmly fixed in their proper position, so that the "hard body" may have been simply a kinked loop of intestine full of feces. The disordered circulation interfered with the functions of all the organs of digestion. Flatulence and ascites raised the diaphragm and further impeded the action of the lungs and heart.[10] The muscles of the back could be strengthened by massage, electricity, and gentle gymnastics, but they quickly reverted to a flabby state if neglected, and the catarrhal condition of the throat required constant treatment because of the condition of hyperemia which could not be corrected. The acne was improved by strict attention to diet and intestinal cleanliness. For the last five years of her life the patient complained frequently of palpitations of the heart, sometimes at night, sometimes on exertion. It is possible to explain these symptoms by the mitral stenosis, since out of seventy-three cases of irregularity of the heart, Lewis found that 52 per cent. were instances of mitral stenosis. In many of these patients symptoms of valvular lesion were absent, the patient complaining of short-windedness, fluttering in the chest or neck, and gastric discomfort, the palpitations sometimes occurring in the middle of the night. Such was the case in my patient, the mitral lesions at times being impossible to define, but owing to the slight sclerosis of the mitral valves, there was at times some stenosis of that orifice, which would cause an increase of the interauricular pressure and eventually a condition of fibrosis of the auricles as well as in the ventricles. Lewis[12] says that it is possible that fibrosis by interfering with the circulation in restricted areas of the musculature sets up a state of irritability. Anemia of the muscle does the same thing, and may also result in extra systoles, and more or less permanent irregular tachy-

10. Brunton, Lauder: Therapeutics of the Circulation, 1908, p. 131.

cardia. "Unexpected death in patients with fibrotic hearts is a well-recognized fact." The aortic murmur, not always present, was caused by an incompetent thickened edge of one cusp of its double valve. Osler[11] thinks that this condition is generally well compensated, and may not shorten life. Broadbent, on the contrary, finds that 40 years is about the limit of life in this condition. Where there is any sclerosis of the aorta, however, there is apt to be a narrowing of the orifice of the coronary arteries. Sudden death may be caused by the blocking of one of these coronary arteries, or there may be a more deliberate sclerosis or a narrowing of the coronaries, which leads to fibroid degeneration of the cardiac muscle and eventually to fatty infiltration or fragmentation of the muscle fibers.

In regard to the degeneration of the coronary arteries, Abbott says:

> I believe that the commonest site for rupture of the cardiac muscle is on the anterior wall of the *left* ventricle [in our case it was the *right*] near the interventricular septum, about the junction of the lower and middle thirds, and the reason that this is the "seat of election" is because this area is supplied by the descending branch of the anterior coronary artery (the artery of the septum), which is a very common branch to undergo thrombosis, or embolism, thus leading to infarction of the supplied area of heart muscle. This vessel has been called the artery of sudden death, because disease of it is so frequently followed by serious results.[13]

We have been told that the left coronary artery supplies the anterior portion of the ventricular septum, and twigs from the right coronary go to the posterior half, with communicating branches passing from one to the other, less work being done by the right coronary than by the left. In cases of great anastomosis in the septum, however, there are few on the outside of the

11. Osler, W.: Practice of Medicine, p. 729.
12. Lewis, Thomas: Paroxysmal Tachycardia, Heart, No. 2, i.
13. Dr. Osler speaks of this in his address on Angina pectoris, New York Med. Jour., 1897, lxiv.

heart;[14] so that possibly here may be one reason for greater strain and consequent degeneration of the anterior coronary artery on the surface of the right ventricle, and its final rupture. In this connection an interesting question arises: Was the intense pain in the legs and abdomen of this patient due to sclerosis of the coronaries and referred to in the abdomen instead of being felt in the heart? Or may there have been a sclerosis of the femorals with intermittent claudication, as well as sclerosis of the aorta and coronaries? The victims of angina pectoris may have marked abdominal symptoms, which may be due to a chronic arteritis in the gastric and mesenteric vessels, as well as to the heart. The radial blood-pressure in my patient never exceeded 140, but it is said that even low blood-pressures may co-exist with early arteriosclerosis. Certainly the intense throbbing in the abdominal aorta ought to have shown a higher pressure there than that in the radials.[15] Osler[16] says that spasm or narrowing of a coronary artery, or even of one branch, may so modify the action of a section of the heart that it works with disturbed tension, and there may be stretching and strain sufficient to arouse painful sensations, like the intermittent claudication of the arteries of the legs in a case of cramp.

Of thrombosis of the coronary arteries Blumer says:[17]

> In view of the situation of the origins of the coronary arteries, their size and the frequency with which degenerative changes attack their walls, it would seem that the chances in favor of thrombosis are much greater than those in favor of embolism.

Stoppage of one of the branches of the coronary arteries does not necessarily lead to sudden death, but as a rule, a thrombus in a large branch is quickly fatal.

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14. Merkel: The Coronary Arteries of the Human Heart, Verhandl. d. deutsch. path. Gesellsch., 1907, Part 10, p. 127; quoted in Am. Jour. Med. Sc., 1908.
15. Osler: Modern Medicine, iv, 285.
16. Osler, William: Lancet, London, March 26, 1910.
17. Blumer, George: Osler's Modern Medicine, iv, 503.

The commonest site of a coronary thrombus is the anterior surface of the apical one-third of the left ventricle and the septum near the apex. Moreover, if the thrombus does not immediately cause the death of the patient, it may cause a necrosis of the cardiac area involved and a rupture of the heart at that spot.

At the autopsy there was thought to be a condition of thrombus of the anterior coronary artery with rupture in three places, but on careful dissection and microscopic examination the arteries were found to be unruptured, and it was the muscle of the right ventricle at a distance of 3 or 4 cm. from the artery, parallel with it, which ruptured, close to the interventricular septum where its circulation was probably the poorest. Abbott writes that this is a rare condition. She says:

"We have four cases of rupture of the heart in this museum, in three of which the seat of rupture is in the situation above described, i. e., the left ventricle wall. Another possible explanation may be that the auriculoventricular bundle of His is distributed so extensively in the septum that disease of the artery supplying the septum may be productive of more serious disturbance than that of the artery in another part of the heart."

There was no sudden pain in my patient's case to note the formation of a thrombus, only restlessness and anxiety, followed by collapse, when the heart ruptured, not only once but three distinct times. The patient's father died probably from thrombosis of the coronaries several days after an operation for appendicitis, and as Blumer[18] suggests, there may be an inherited tendency to the production of thrombogen or thrombokinase. The effect of ligation of the coronary artery must be similar to thrombosis. Lewis says:[19]

In the case of the right coronary, the area devascularized includes the right auricle and the greater part of the right ventricle. The muscle involved blanches and then becomes livid. The right auricle continues to beat less and less strongly,

18. Blumer: In Osler's Modern Medicine, iv, 504.
19. Lewis, Thomas: Auricular Fibrillation and Its Relationship to Clinical Irregularity of the Heart, Heart, 1910, No. 4, i, 368.

while the ventricle follows even less strongly to final fibrillation. Tachycardia was obtained in nine out of the twelve cases of right coronary artery ligated, cardiac irregularities most often following obstruction of this artery, and paroxysms occurring in from fifteen to sixty minutes after interference with the vascular supply, the paroxysms varying from a few seconds to thirty-five minutes in duration. But if tachycardia is caused by a lesion in the cardiac muscle of the right ventricle itself, independently of nervous control, heart-block and a stop of the auricular beat can be also caused by irritation of the vagus.

Therefore, in this case, the anemic condition of the cardiac muscle, or of the bundle of His, caused by a lack of blood-supply from the sclerosed right coronary artery, may have been the cause of the palpitations and discomfort, while the dilatation of the stomach and intestines may have produced pneumogastric irritation which further increased the cardiac irritability, resulting in fibrillation of the ventricle and sudden death from ventricular exhaustion. The rate of rhythm of the ventricular contraction varies from 140 to 420. In my patient the pulsation in the left carotid was from about 160 to a beat too rapid to count, followed by sudden stilness. At the autopsy the blood found in the pericardial sac amounted to only 60 c.c., too little of itself either to stop the heart by pressure or anemia; many a stab wound of the heart being larger than all of the ruptures in the right ventricle. Therefore, it seems to me that we may be justified in attributing death ultimately in this case, to the trouble in the sinoventricular conducting system[20] rather than to the rupture, and that neither the patent ductus arteriosus nor the aortic stenosis would have been incompatible with long life. In all the cases of heart-block or extrasystole which have come to autopsy, there have been shown

20. Retzer has renamed the bundle of His the sinoventricular conducting system. This he considers a neuromuscular apparatus possibly connected with the sympathetic ganglia, the end organs of the conducting system being surrounded by a plexus of nonmedullated nerves. Retzer: Anat. Rec., ii, 149; Johns Hopkins Hosp. Bull., 1908, p. 208.

either gummata, anemic necrosis on account of thrombosis of the nutrient arteries, fibrosis, new growth, atheroma, or fatty infiltration.[21] The common cause is the same, i. e., interference with the conducting bundle (the auriculo-ventricular bundle), or its node.[22] This is probably one of the reasons why digitalis failed to be of service in the case in question, and explains the symptoms of fluttering or big thudding beats, or the long pauses often complained of by the patient, when taking this remedy, and which were dismissed as being irregularities due to indigestion and not to organic change in the heart. In a recent case of rheumatic endocarditis, Mackenzie[23] observed a delay in the *a-c* interval, which was greatly increased by digitalis so that several ventricular beats dropped out altogether, and the pulse became markedly irregular. Stimulation of the vagus was also capable of converting delay of auriculoventricular conductivity into actual heart-block. Digitalis distends the ventricles, and on contracting they drive out a much larger wave of blood through the aorta than is normally sent out; but in raising general blood-pressure, digitalis could not affect the sclerosed coronaries, while at the same time the pressure in the aorta could not be raised, owing to its stenosis and unhealthy condition. Moreover, in such a case as this, in which pressure was not normal, there may have been a lesion in conductivity which digitalis would aggravate, and therefore thrombosis and further coronary degeneration would be favored by this vasoconstricting remedy. In condition of weakened heart with increased blood-

21. Thomas Lewis in a recent article on auricular fibrillation has formulated the following data as to the action of digitalis. "Digitalis retards the ventricular rate in clinical auricular fibrillation by enhancing a previously existing auriculo-ventricular heart-block. The rapid and irregular impulses showered on the ventricle from the fibrillating auricle are hindered in their passage from one chamber to the other by the action of drugs of this class. The influence of digitalis is exerted, directly or through the vagus, on the junctional tissues between auricle and ventricle."

22. Brown, W. L.: Physiological Principles in Treatment, p. 251.

23. Carter, Alfred H.: Article on Heart Disease, Quoted in the Internat. Med. Ann., 1908, p. 288.

pressure, strophanthus, which is not so much of a vasoconstrictor as digitalis, is considered useful, but in the case in question this drug quickly caused pain in the stomach and nausea. Apocynum was not tried, and nitroglycerin did not seem to be indicated. For these reasons it was thought best to keep the patient at comparative rest and give her the mildest of Schott's resistive movements plus gentle massage of the extremities. Massage to the abdomen was soon abandoned because it was found to give her pain and to irritate the heart through its stimulation of the splanchnics. When these remedies failed I superintended artificial Nauheim baths at a temperature of 95 F. for five minutes. The first two baths reddened the skin, improved the pulse, and seemed productive of general amelioration of the symptoms; the two following baths caused no good reaction and were consequently discontinued as being too fatiguing.

Being somewhat baffled in treating the heart, we turned our attention to the bowels, which were very sluggish, and to the kidneys, which were doing half-work, the edema being stationary. For the bowels calomel was given on alternate days, followed by concentrated magnesium sulphate, in the hope of producing watery movements. Theobromin was given as a diuretic, which for a time nearly doubled the output of urine, but it too seemed to irritate the stomach, and caused a great disinclination for food. Strychnin, which acts on the centers, was contraindicated, because the nerves, being already irritable, responded too freely. Epinephrin and ergot, peripheral constrictors, which combat vasomotor had paralysis, no effect on the coronary arteries since they have no vasoconstrictors, although useful in shock in which the splanchnics are dilated and are able to respond to the constriction. Moreover, the vasomotor nerve, the depressor which prevents too great fulness of the blood-vessels, does not work when the

heart is dilated because the splanchnics are probably at the same time injured, and incapable of response.

During all this time, despite the futility of treatment, the patient's color was very good. She was healthy looking, cheerful, interested in everything but herself, and never anxious as to her ultimate recovery, an optimism which was shared by all the consultants who examined her, as well as by me, up to the last thirty-six hours, when all the disagreeable symptoms rapidly increased, the most troublesome of all being the continuous laryngeal irritation, and which no hypodermics or any form of treatment could arrest until the final rupture of the heart and death. In such a case as this we could hardly call death sudden, for it had been indicated for eighteen hours, and although there was fatty infiltration of the muscle and fragmentation of muscle cells near the rents, and a packing of non-nucleated blood corpuscles at the edges of the ruptures, the patient's general condition seemed so good that possibly in a little longer time a new collateral circulation might have been established, and the wounds healed, if the sinoventricular apparatus had not been interfered with.

The kidneys and liver shared in the general discomfort of this patient for the last two weeks of her life. The liver may be looked on as a sponge-like safety-valve to the heart, which works to its own destruction until edema and ascites occur. If death follows soon, the liver shows its engorgement; if death is postponed, the liver shrinks and shrivels. The edema and ascites in this case remained stationary, and the liver was not noticeably enlarged or fatty.

The condition of the kidneys and their function in this case is best described by Osler. "There is a great lessening in the total amount of urine excreted; darker color, strongly acid reaction which is caused by sarcolactic acid made from the poor arterial blood, and slight albumin." In other words, a mild nephritis, with

thickening of the wall of the arteries such as was found at autopsy.

In all the 100 cases of sudden death from rupture of the heart, reports of which were collected by Quain,[24] the rent was most frequently in the anterior wall of the left ventricle near the septum. In this patient the dilated and hypertrophied right ventricle, near the septum, was the seat of rupture, and possibly someone may be able to suggest why death was less sudden when the break was on the right side of the heart than on the left.

It is evident that we have one great lesson to learn from the history of such a case as this, namely, the necessity of early diagnosis of congenital defects in the heart, with consequent insistence on a hygienic life, protection as far as possible from infectious diseases (including rheumatism and common colds as well as influenza and children's diseases), and avoidance of nerve or muscle strain. Careful study of cardiac murmurs should teach us to know congenital anomalies, in order to differentiate them from endocardial inflammatory changes in the valves; and wherever it is possible, the diagnosis should be confirmed by autopsy and the cases studied and published for the benefit of the medical profession in the care of similar cases.

ABSTRACT OF DISCUSSION

Dr. Wilder Tileston, New Haven, Conn.: I should like to emphasize the paralysis of the recurrent laryngeal nerve. Pressure by a dilated ductus arteriosus must now be added to the list of possible causes of recurrent laryngeal paralysis. A few years ago v. Schroetter, jr., of Vienna, reported a case of patent ductus with laryngeal paralysis, exactly similar to Dr. Mead's. At that time this was the only case of the sort to be found in the literature.

24. Osler: Modern Medicine, iv, 202.

A CASE OF DIFFUSE, PURULENT, VENTRICULO-SEPTAL MYOCARDITIS WITH ADAMS-STOKES' SYNDROME *

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The subject of suppurative myocarditis has received some attention from ancient writers, since Whittaker[1] states that Galen described this malady in gladiators and Benevenus and Bonetus have also described abscesses in the walls of the heart. Later, Laennec and Meckel cited similar cases.

These cases of suppurative myocarditis are called "myocarditis purulenta" by Aschoff,[2] who shows that they are usually produced by ulcerative endocarditis, intracardiac thrombosis, pericarditis and septic infarction and abscess formation in cases of general pyemia. It will be seen that these purulent infiltrations or abscesses in the heart muscle are secondary processes caused by an antecedent infection. The case we shall later describe is a primary condition and cannot, therefore, be compared to the above mentioned processes.

The condition known as acute interstitial myocarditis, which follows such infectious diseases as diphtheria, scarlet fever and rheumatism, first described by von

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1. Whittaker: Twentieth Century Practice of Medicine, 1905, iv, 127.

2. Aschoff: Pathologische Anatomie, Jena, 1909, ii, Special Part.

Hayen,[3] also differs from our case, since it is characterized by an infiltration of lymphocytes, plasma cells and fibroblasts, while the polymorphonuclear leukocytes are absent.

Before describing our case in detail we wish to cite a case of acute purulent interstitial myocarditis following subacute rheumatism which was described by Freund[4] in 1898.

This patient had a frequent pulse, a rise of temperature, precordial pain and delirium. The autopsy showed a flabby heart containing yellow dots and lines, and the microscopic examination revealed a diffuse inflammation with polymorphonuclear leukocytes combined with scattered hemorrhages. The blood-vessels were filled with leukocytes and the small veins contained thrombi. The muscle fibers contained vacuoles; the nuclei were elongated, thickened, fragmented and at times absent, and the cross-striations were often obscure, while the individual fibrils seemed separated one from another. Toward the endocardium they showed fatty degeneration.

The above case is the only one we have been able to find in literature of a true, diffuse, interstitial, purulent myocarditis, but we have collected a few typical instances of circumscribed abscess formation in the heart muscles. Carnas[5] states that abscesses of the walls of the heart have been most frequently observed in pyemia and ulcerative endocarditis. In certain cases there are remissions followed by relapse which give a subacute or chronic character to the disease. Laking[6] describes a case of many months' illness with sudden death, which showed two long-standing abscesses in the apex of the left ventricle, and Roth[7] has shown that these abscesses may undergo calcareous transformation. Chance[8] and Howitt[9] both report abscesses of the heart in children,

3. Von Hayen: Arch. de physiol. norm. et path., 1869-70, iii, 81.
4. Freund: Berl. klin. Wchnschr., 1898, xxxv, 1077, 1106.
5. Carnas: Myocardite primitive suppurée du septum, Loire méd., 1892, xi, 113, 120.
6. Laking: Saint George's Hosp. Rep., 1875, vii, 361; Rev. d. sc. méd., 1876, i, 589.
7. Roth: Cited by Ziegler, Lehrbuch der speciellen pathologischen Anatomie, Jena, 1887.
8. Chance: Lancet, London, May 16, 1846, p. 548.
9. Howitt: Lancet, London, June 20, 1846, p. 684.

and nine out of ten cases occur before the thirtieth year. Formad[10] reported a case of abscess of the heart about the size of a large bean with accompanying purulent myocarditis, and it is interesting to note that this condition may develop from a circumscribed abscess. Banks[11] also has described an abscess the size of a pigeon's egg in the left ventricle.

Abscess of the heart follows pyemia or septic endocarditis and is characterized by angina-like symptoms, dyspnea, gallop rhythm, dicrotic pulse and temperature, and Loin[12] states that this condition may be distinguished from septic endocarditis by a more rapid pulse in the former condition.

The association of heart-block with infectious diseases has recently been established. The few cases thus far reported have been reviewed by Peabody,[13] who reports an additional case. Some of the patients recovered. Autopsies have revealed various lesions of the bundle of His, such as anemic necrosis of the muscular septum in the region of the bundle, cellular infiltration, fibrous degeneration with a calcareous nodule pressing on the bundle; and James[14] has reported a case in which the bundle of His was completely destroyed by an ulcer in the interventricular septum due to a streptococcus septicemia.

Other conditions which may produce heart-block and Adams-Stokes' syndrome are syphilitic gummata and scar formation, calcareous deposits, fatty infiltration, septic and benign infarction and fibrous tumor of the bundle of His, as we have already described in a former article.[15]

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10. Formad: Tr. Path. Soc. Philadelphia, 1891-3, xvi, 80.
11. Banks: Proc. Path. Soc., Dublin, 1852-53, p. 27.
12. Loin: Ann. Soc. d'anat. path. de Bruxelles, 1880-81, Bull. 30, p. 31.
13. Peabody, F. W.: Heart-block Associated with Infectious Diseases, Arch. Int. Med., 1910, v, 252.
14. James: Am. Jour. Med. Sc., 1908, cxxxvi, 469.
15. Beck and Stokes: A Clinical and Pathologic Study of a Case of Adams-Stokes Disease, Arch. Int. Med., 1908, ii, 277.

We regret that we were unable to obtain any pulse tracings in the case the report of which follows, but the patient was under observation only for several days in the hospital, during which time the sphygmograph was being repaired. Nevertheless, we are convinced that he suffered from heart-block with Adams-Stokes' syndrome. The case is unique because of its association with the rare condition of primary purulent myocarditis.

CASE REPORT

CLINICAL HISTORY

Patient.—J. C., a man aged 67, by occupation a street-cleaner. His history is unimportant. In early childhood he had measles, scarlet fever and mumps. Apart from these maladies he enjoyed remarkably good health until his thirtieth year, when he contracted syphilis. He developed the usual characteristic secondary symptoms, for which he received several months' treatment. He was always employed at heavy, laborious work. In his earlier days he was strongly addicted to the use of alcohol, mostly in the form of whisky. For the past twenty-five years he drank more moderately.

Present Illness.—He continued in good health until seven months before his admission to the Mercy Hospital. At this time he began to have vertigo and syncope with epileptiform seizures. These attacks came on abruptly, frequently without premonition, at other times with a brief aura, consisting of a sense of smothering, scotoma and tinnitus aurium. The patient sank rapidly into a state of semiconsciousness, which was followed by clonic spasms of the facial muscles on the right side and tingling and formication in both upper extremities. Other associated symptoms were vasomotor disturbance, oppressive sensation in the epigastrium, with pain which radiated to both arms, and intense dyspnea. The entire seizure lasted only a few minutes. These attacks came on very frequently. They were usually single, but sometimes five or six followed in close succession; excitement or physical exertion had a tendency to produce them. For this reason the patient had been unable to follow his vocation for the past seven months. Three months after the onset of the attacks a cough developed, which was accompanied with a slight expectoration. Dyspnea on slight exertion became an annoying symptom. Later he noticed enlargement of the veins in his legs, which subsequently became varicosed. There was no edema. He had a constant feeling of

pressure in his epigastrium and dyspeptic symptoms were marked. On March 25, 1910, on the advice of his physician, Dr. C. F. Blake, he was sent to the hospital.

Physical Examination.—This revealed the following condition: The patient looks fairly robust, is well developed and in a good state of nutrition. Mentally he is apathetic, inclined to stupor and talks incoherently, but, when aroused he appears nervous and apprehensive and responds readily to inquiries in a perfectly rational manner. The face is pale, the lips slightly cyanosed and the conjunctivæ anemic and injected. The pupils are equal and react sluggishly. The tongue is coated and flabby with marginal indentation. The mucous membrane of the tongue and buccal cavity show a slight degree of cyanosis. There is a small patch of alopecia of the scalp, and the hair and eyebrows come out readily. The jugular bulbs and the superficial veins of the neck are distended and pulsate. The chest is somewhat emphysematous in type. Breathing is irregular and, at times, Cheyne-Stokes in character. Percussion of the lungs shows hyperresonance over the anterior and lateral aspects of the chest and over the upper half posteriorly. The bases of both right and left lung are moderately dull. Fremitus is generally decreased. On auscultation emphysematous breathing is heard over the entire chest and a few dry scattered râles are heard.

Heart: The maximum apex impulse is in the fifth interspace at the mammillary line. There are no abnormal areas of pulsation. Relative cardiac dulness extends 1.5 cm. to right of the right sternal border and the distance from the mid-sternal to the left border at the apex measures 9 cm. Dulness begins above at the lower border of the second rib. There are no cardiac murmurs at the apex; both sounds are clear and distinct. The first sound, however, is not entirely normal, as it lacks the so-called booming quality which is a distinctive feature of the mitral systolic sound. The aortic and pulmonary first sounds are almost inaudible. A reduplication of the second sound is heard at the aortic and pulmonary areas, and also at an area corresponding to the junction of the fourth interspace and left sternal border. Bradycardia is pronounced and the cardiac rhythm is fairly good. There are from 44 to 46 apex-beats per minute, while there are from 86 to 94 jugular pulsations, denoting practically a 2 to 1 rhythm. The radial pulse is likewise slow (46 per minute), but the rhythm is good and pressure is minus. The ratio between the auricular and ventricular systole is disturbed when the patient exercises.

The blood-vessels are somewhat thickened, but no more so than one would expect to find in a man of the patient's age. With the exception of double inguinal hernias the abdominal examination is negative. The superficial veins of the lower extremities are engorged. Reflexes are not disturbed. There is a slight enlargement of the cervical and inguinal glands.

Urine: Specific gravity, 1,013; traces of albumin; otherwise negative.

Course of Disease.—March 28: The patient had several seizures during the night, following each other in close succession, and to-day he appears exhausted and drowsy. He has Cheyne-Stokes breathing and voids large quantities of urine.

March 29: Slept well during night and shows a general condition of improvement. Radial pulse is fairly regular but slow. Jugular pulse well marked. Two pulsations occur to one radial.

March 30: Radial pulse, 43; jugular, 86. Forced exercise in bed produced an acceleration of the venous pulse to 98, but had no effect on the radial pulse. The following records taken during the day show the relation between the radial and jugular pulses:

Time.	Radial.	Jugular.	Time.	Radial.	Jugular.
9:30 a. m.....	48	99	12:00 m.	46	94
10:00 a. m.....	46	84	12:30 p. m.....	44	90
10:30 a. m.....	50	104	1:00 p. m.....	48	96
11:00 a. m.....	48	98	1:30 p. m.....	42	90
11:30 a. m.....	52	90	2:00 p. m.....	50	96

March 31: Patient felt comfortable during the early part of the night, but later in the night he ventured out of bed and was found in the toilet with an acute paroxysm. He had another paroxysm shortly after returning to bed, from which he quickly recovered. Several hours later he was found dead in bed.

During his entire stay in the hospital the patient's temperature was normal.

GENERAL AUTOPSY REPORT

Body Section.—Lungs show some edema and congestion. Pericardial sac filled with a bloody fluid. Heart somewhat enlarged. Arteries show some sclerosis. Liver about normal in size, but showed chronic passive congestion. Spleen normal. Right kidney much enlarged and several small cysts on its surface filled with a watery fluid. Left kidney enlarged and both showed chronic nephritis. Stomach showed marked congestion and acute gastritis.

Owing to an unfortunate accident no microscopic sections were made from the viscera, other than the heart, but it may be taken for granted that there was no acute purulent condition present and that the sections would have shown only a chronic nephritis and an acute congestion of the gastric mucous membrane.

Bacteriologic Examination.—No cultures were made, but stained specimens showed a few pneumococci in the purulent areas of the heart muscle.

EXAMINATION OF HEART

The heart is somewhat enlarged, weighing 450 gm. The measurements are as follows: Thickness of left ventricle midway 18 mm.; length of left ventricle 8.5 cm.; aorta, just above valves 8 cm. in circumference; interventricular septum 9 mm. thick. Right side of heart: right ventricle 8 mm. thick; length of right ventricle 8 cm.; pulmonary artery just above valve 5.5 cm.

The papillary muscles of the right and left ventricles are flattened. The heart muscle is reddish brown in color, and, on cutting through the interventricular septum, near the auriculo-ventricular septum, fine yellowish streaks can be seen. On making a flat section of the muscle of the left ventricle opposite the interventricular septum, small grayish streaks and small reddish dots are apparent in the muscular substance which has been laid open. The valves are normal. The aorta contains a few small yellowish plaques just around the entrance of both coronary arteries, and there are numerous smaller plaques scattered over the intima of the rest of the aorta.

Coronary Arteries.—Both coronary arteries were dissected out to the ramification of their finest branches, and the general condition is as follows:

Left Coronary Artery: The main artery, the left descending branch and the circular branch all contain numerous bulbous thickenings, giving the artery an irregular, beaded or nodular appearance. To the touch, the entire artery is much firmer and harder than normal, and the irregular miniature sausage-shaped nodules have the feel of hard bony tubes. A fine probe measuring 1 mm. in thickness can be passed through the circular branch and also through the descending branch to a distance of 6 cm., but the lumen is evidently narrowed, as the probe passes with difficulty. On opening the artery, the intima is seen to contain numerous irregular yellowish elevations, most of which contain a soft pultaceous yellow material, or a much firmer calcareous deposit forming thick plates.

Fig. 1.—Heart, showing the situation of the various blocks from which the sections were made. These are numbered as in the text. These blocks of tissue were cut out of the heart in order to obtain cross-sections of the bundle of His.

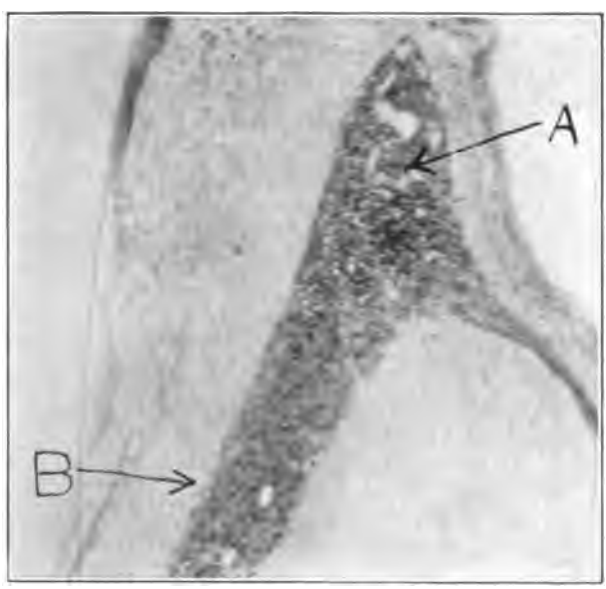

Fig. 2.—Cross-section of the bundle of His at A, in which there were numerous hemorrhages. The auricular septum is above and the ventricular septum below, the bundle running in a groove between its two septa. The thick bundle passing down to the left is the bundle for the right ventricle and the thinner branch nearer the endocardium is the branch for the left ventricle.

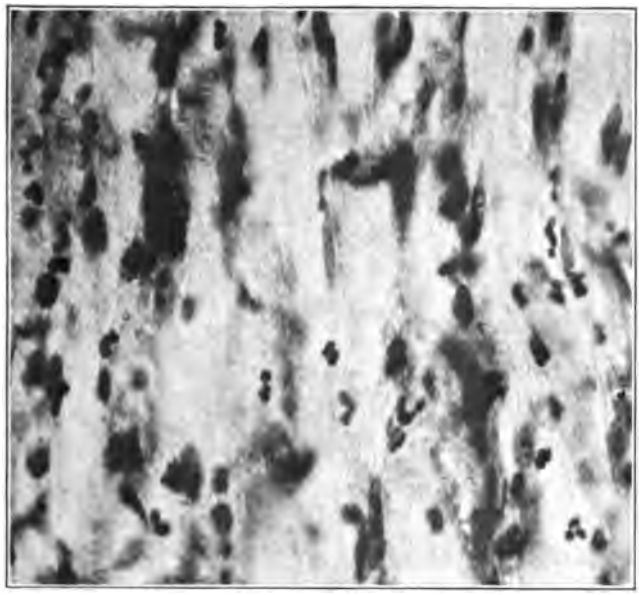

Fig. 3.—From a photomicrograph taken at B in Figure 2. It shows diffuse purulent infiltration, fragmentation, atrophy and hyperchromatosis of the nuclei of the heart muscle.

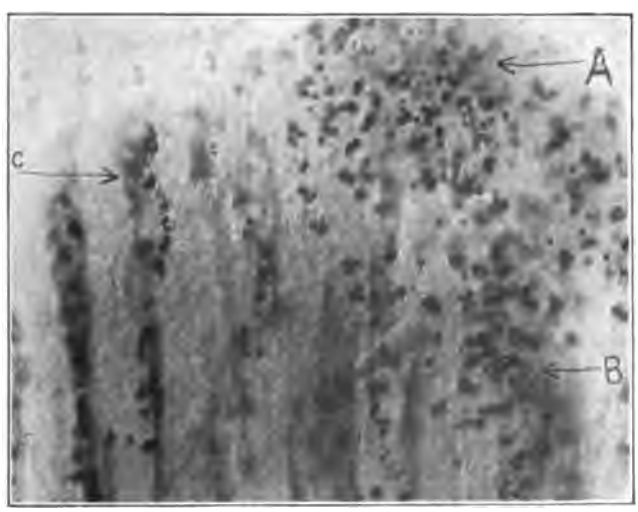

Fig. 4.—Area of necrosis with intense nuclear fragmentation and purulent infiltration at A. At B the general purulent infiltration is seen, and at C this purulent infiltration pursues a linear course between the individual muscle fibers.

Right Coronary Artery: This artery does not show the same nodular condition, but presents rather a general indurated, cord-like, leathery feeling. On opening up the artery, there are a few small yellowish plaques containing a soft, pultaceous, yellow, cheese-like material, but there are no calcareous deposits. The intima seems universally thickened, presenting a firm, tough, thickened tissue. A probe 1 mm. in thickness passes 4 cm. through the main artery, where it is abruptly stopped by an adherent thrombus which extends for a distance of 3 cm. in the descending branch supplying the right ventricle.

Histopathology.—Before describing the microscopic changes present in the heart, it is necessary to describe the situation of the various blocks of tissue from which the sections are made, and this can best be explained by referring to the photograph of the heart which is seen in Figure 1.

Section 1 was made from a block of tissue bounded to the left by the endocardium of the left ventricle, to the right by the endocardium of the right ventricle, and above and below, by the fibromuscular wall of the auricular septum. The section, therefore, passes from above downward directly through the center of the fossa ovalis, and includes the muscular structure of the auricular septum for a considerable distance below the fossa. It, therefore, would show a cross-section of any of the rootlets of the bundle of His, taking their origin from the region of the septum. The area formerly occupied by this block of tissue is indicated by the number 1 which will be found within the limits of the first set of white lines.

Sections 2, 3, 4, and 5, were made from blocks of tissue which include the horizontal course of the bundle of His, showing, therefore, cross-sections of the bundle. They form triangles whose apices are represented by a point just above the auriculoventricular fibrous ring, and whose sides are formed by the endocardium of the right and left ventricles. The bases are formed by lines passing from the left to the right ventricle directly through the interventricular septum. The situation of these blocks is indicated in Figure 1 by the numbers mentioned above, and their distal planes are designated by the white lines.

Sections 6, 7, 8 and 9 are made from blocks which follow a line perpendicular to the apex, which begins at the base of the last section, and ends at the apex. These blocks pursue the general course of the two branches of the bundle of His for the right and left ventricle, and the sections, therefore, show these branches in an oblique or horizontal plane. The white lines show the distal limits of each block, while the numbers show the situation of these blocks.

Sections 10, 11, 12 and 13 are taken from blocks which pursue a gentle curve around the very limits of the auriculo-ventricular septum adjacent to the apex, and they end at the very tip of the apex of the heart. They are numbered by black figures, and the black lines indicate the limits of each block of tissue.

Microscopic Examination.—No. 1: This section, passing through the muscles of the auricular septum, the fossa ovalis and the lower portion of the auricular wall, shows a few strands of the bundle of His, taking their origin from the thin wall of the fossa. The nuclei are larger than the rest of the heart muscle, and the muscle fibers are separated and surrounded by a connective tissue containing many fibroblasts, lymphocytes and a few polynuclear leukocytes.

No. 2: This is a section through the proximal end of Segment 2, showing the auricular septum, the ventricular septum and the auriculoventricular groove containing the bundle of His. The bundle of His and the connective tissue around it are infiltrated by many polynuclear leukocytes. The muscular structure of the ventricular septum, especially that near the endocardium of both ventricles, presents a remarkable appearance. There is a diffuse purulent infiltration of the muscles separating individual fibers or groups of fibers. Many of the fibers show necrosis, and there are also groups of leukocytes which show much nuclear fragmentation. Other groups of leukocytes form elongated abscesses.

No. 3: Conditions are practically similar to those found in No. 2.

No. 4: This shows the thin connective tissue septum of the auricle with many connective tissue cells but no muscle fibers. Below the septum in the auriculoventricular groove, the bundle of His can be distinctly seen, together with its branches for the right and left ventricles. The central bundle itself contains many scattered hemorrhages, and the branches for the right and left ventricle soon become involved in the general purulent infiltration, described above. This purulent infiltration can also be seen scattered in certain areas throughout the entire septum, and these areas show intense granular degeneration of the muscle fibers. The purulent infiltration is much more intense just beneath the endocardium of both ventricles, and this infiltration often forms a network between the muscle bundles of degenerated necrotic muscle fibers. The branching of the bundle is well seen in Figure 2.

No. 5: In this section the central bundle has apparently disappeared but the left branch is still visible, and at some distance from the bifurcation, it shows moderate purulent infiltration. There is also marked purulent infiltration of the

entire septum in the lower half of the section, especially towards the endocardium of the right ventricle.

No. 6: This section is made from a series of blocks which are perpendicular to the apex and which follow the general course of the two bundles of His, as they course downward in the ventricular septum towards the apex. It is impossible to locate the cross-section of any particular bundle of muscle fibers which would correspond to either of the branches of the bundle of His, and there is no marked purulent infiltration of the muscle in this section. The thickened endocardium does show a slight infiltration with polynuclear leukocytes and lymphocytes, and there are a few similar groups of cells scattered through the section. There are areas of hemorrhages scattered through the muscular structure, and the blood-vessels are crowded with leukocytes and lymphocytes.

No. 7: This section shows areas of intense hemorrhage together with coagulative necrosis of the muscle fibers, and there is an increase of connective tissue elements between the muscle bundles, indicating a beginning chronic interstitial myocarditis, and some of these areas of coagulative necrosis show marked nuclear fragmentation.

No. 8: In this section through a plane which is nearer the apex, there are, again, areas of marked purulent infiltration with necrosis of the muscle fibers. There is also some chronic interstitial myocarditis and scattered hemorrhages.

No. 9: This ends the series made from blocks approaching the area of the apex, and the conditions are similar to those described in No. 8. A section through several large papillary muscles fails to show any purulent infiltration, but the intense congestion of the capillaries in certain areas of the heart muscle is marked.

No. 10: This section is taken from the first of a series of blocks which pursue a gentle curve around the limits of the auriculoventricular septum ending at the apex. The heart muscle shows extensive necrosis, numerous hemorrhages and congestion of the capillaries, and there is slight, scattered purulent infiltration. The numerous papillary muscles do not show any abnormal changes. A branch of the coronary shows a greatly thickened intima containing numerous connective tissue cells.

No. 11: This tissue shows extensive areas of necrosis and hemorrhages, and these areas are infiltrated by small mononuclear lymphocytes, singly or in groups, and the blood-vessels also contain increased number of lymphocytes.

No. 12: This section is principally marked by extensive areas of hemorrhage and some chronic interstitial myocarditis.

Summary.—It will be seen by reference to Figure 1, that the sections are taken from blocks beginning at the fossa ovalis in the auricular septum, and describing a semicircle passing outward along the horizontal course of the bundle of His, then downward through the ventricular septum, and finally describing a gentle curve, the semicircle ending at the very tip of the apex.

There were no pathologic changes found in that portion of the auricle from which the bundle of His takes its origin, but after the bundle has entered the auriculoventricular groove, it is beset by numerous hemorrhages, and its two branches show moderate purulent infiltration. The rest of the muscular structure of the septum shows marked purulent infiltration in the linear areas beneath the endocardium of both of the ventricles and in scattered masses throughout the tissue. There is also marked arteriosclerosis.

Sections From Other Portions of the Heart.—In addition to those described above, sections were made from various other portions of the heart in order to study the extent of the purulent infiltration and the condition of the blood-vessels.

Those of the first set were made from the left auricular appendix, the septum between the auricles, the wall of the right auricle and the musculi pectinati of the right ventricle. The left auricle shows no abnormal changes, but the wall of the right auricle with its musculi pectinati shows a few polynuclear leukocytes in single rows, or small groups, and the nuclei of many of the muscle fibers are shrunken and irregular in size and shape.

Another set of sections was made from the wall of the left ventricle at the left apex, from four separate areas in this wall opposite the septum, and running from the base to the apex, through the papillary muscles, and from the interventricular septum. The first section near the apex shows an adherent antemortem clot attached to the endocardium by means of fibrin. There are many endothelial cells and fibroblasts entering this fibrin in an attempt at organization, and the endocardium is thickened and infiltrated by leukocytes, red blood-corpuscles and fibroblasts. The clot contains masses of fibrin and polynuclear leukocytes and fibroblasts. The muscle fibers next to the endocardium contain numerous large vacuoles, only a mere shell remaining, and the nuclei are frequently shrunken. There is no diffuse purulent infiltration. The five sections from different portions of the left ventricle opposite the septum do not show any marked changes, but the muscle fibers of the papillary muscles near the endocardium show vacuolization. The septum at the apex shows no marked changes, except fatty infiltration near the pericardial surface.

The right coronary artery 6 mm. from the mouth of the aorta shows an interesting condition. The intima is greatly thickened, measuring from 2 to 10 times the thickness of the media adjacent to it, which shows marked atrophy. It contains a moderate number of fibroblasts and two large irregular areas of calcareous deposits. The lumen is completely occluded by a thrombus consisting mainly of red blood-corpuscles and fibrin, but containing groups of organizing fibroblasts and a few polynuclear leukocytes. This thrombus is adherent to the intima from which the endothelium has become detached. A smaller branch of this coronary artery also shows the same thickened intima, and the lumen is reduced to a small irregular channel. The adventitia contains numerous fibroblasts filled with small brown granules of blood pigment, and the muscle fibers of the media show great atrophy. The intima contains scattered polynuclear leukocytes, granular masses of lime salts, and fibroblasts. The same artery nearer the aorta also contains an adherent thrombus of the intima, and shows great thickening of the intima and, just where this is attached to the thrombus, it is highly infiltrated by leukocytes.

SUMMARY

The clinical history of this case indicates that the patient had been suffering from syncopal attacks for a period of seven months. It is difficult to account for these earlier attacks unless we can believe that there were recurrent purulent infiltrations of the bundle of His with damage to the muscle fibers. We found no other lesions of the bundle of His and can only report the patient's condition for about a week prior to his death, together with the discovery of an acute primary purulent infiltration involving the bundle of His.

We desire to thank Dr. H. W. Stoner for the photograph and photomicrographs, and Dr. J. J. O'Malley for assistance rendered.

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A STUDY OF A CASE OF HEART-BLOCK

WITH ALTERNATION OF THE SYSTOLIC AND DIASTOLIC JUGULAR WAVES

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So much has been written in the past few years about heart-block that the report of a single case can no longer be considered worth while. My reason for reporting the present case is that it presents a feature which, so far as I can learn, has not yet been described. It is apparent from the wide diversity of symptoms and of tracings in the cases constantly being reported that not all cases of heart-block are alike and there is certainly much still to be learned about the clinical picture the disease presents. Each case recording some new point adds to the sum of our knowledge.

Briefly stated, the phenomenon essential to the diagnosis of heart-block is the dissociation of the rates of pulsation of the auricles and ventricles. This is generally attributed to an affection of the bundle of His along which travels the stimulus from auricle to ventricle. The block may be complete, in which case the auricular and ventricular rates are entirely different; or it may be partial, as in my case, when some of the auricular stimuli pass through to the ventricles. The peculiar feature which my patient presented in addition was an alteration of the systolic wave, (v), and the diastolic wave, (h), appearing in the jugular pulsations.

REPORT OF CASE

History.—The patient, a white male, aged 75, was admitted to the Touro Infirmary, New Orleans, May 17, 1909, complaining of headaches, dizziness, constipation, belching, and going to sleep. His complaints were of four years' standing. His family history was entirely without interest for the present inquiry. He had always been perfectly well and did not remember any other than the most trifling illness. He had had gonorrhea thirty years ago. He chewed and smoked tobacco moderately and seldom drank alcohol.

Examination.—The physical examination showed a well-developed and well-nourished and well-preserved man. The heart was practically normal in size, the apex being just inside the left nipple and the right border at the right border of the sternum. No murmurs were to be heard. There was a mod-

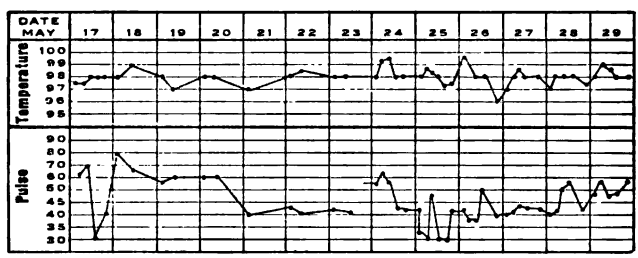

Fig. 1.—Showing the variation in the pulse; record taken every four hours.

erate peripheral arteriosclerosis. The urine showed no abnormalities. The pulse showed a considerable range in frequency, beating sometimes at the rate of 30 to 35 and at other times as rapidly as 70 to 75. The heart-rate, counted at the apex, corresponded always with the radial pulse. The variation in the pulse is shown in the accompanying chart (Fig. 1), on which is recorded the rate taken every four hours. On June 12, 1909, he had "a spell of dizziness and almost lost consciousness for a second." He was taken to his room and there lay down. Shortly afterward his pulse was found to be 36 and weak. Heart-sounds could not be heard. After two or three minutes the pulse jumped to 72 and became stronger. A few weeks after his admission to the hospital he was transferred to the Julius Weis Old Folks' Home, which is a department of the Touro Infirmary, and has remained under observation during the year which has elapsed. He has continued to complain of frequent dizziness but there have been no more syncopal attacks.

I was fortunate enough on several occasions to get tracings at the moment of the change in his pulse-rate. Such a tracing is given in Figure 2. This tracing was made October 17, 1909. At the beginning of the tracing the auricular rate was 66 while the ventricular was 33. Every other stimulus from the auricle, therefore, was blocked. The *a-c* interval (the time between the auricle beat and the ventricle beat) was 1½ (expressed in fifths of a second). The normal interval is about one-fifth of a second. At the point marked *x* the block suddenly ceased and all the auricular stimuli passed through to the ventricle. The rates of the auricles and of the ventricles were now both the same, 60. The *a-c* interval continued to be one and a half fifths.

Figure 3 shows a tracing taken Feb. 20, 1910. Here there is a similar block of every other auricular stimulus. The ventricular rate was 31 and the auricular rate 60. The *a-c* interval was somewhat longer than on the previous occasion, being one and two-thirds as compared to one and a half. Neither of these tracings presents the unusual alternation of the systolic and diastolic waves. This is seen apparently only in tracings where there is no heart-block. A good illustration is given in Figure 4. Here it is very easy to see in the jugular (the upper tracing) that the waves *v* and *h* are alternately high and low. Thus in cycles 6 and 8 they are high and in 7 and 9 they are low. The alternation is clearer in Figure 5, where the enlargement is greater. The wave *h* is not lettered here but it is the wave following immediately after the *v* and it will be observed that its alternation corresponds to that of the *v* wave. In both of these tracings there is no block, although the slowness of the radial pulse would have led one to suspect its occurrence. The rate of both auricles and ventricles was 46. The delay of the auricular stimuli is evidenced by the increased *a-c* interval—two-fifths of a second.

Fig. 2.—Pulse-tracing taken at the moment of change of pulse rate. At the beginning of the tracing the auricular rate was 66, while the ventricular was 33, afterward 60, showing block of every other stimulus from the auricle. No alternation of any waves: *a*—*c*=1½; continues the same after disappearance of block.

Fig. 3.—Tracing showing similar block of every other auricular stimulus. Auricular rate 60; ventricular 31.5; *a*—*c* interval=1⅔; no alternation of waves.

Fig. 4.—Tracing made when there was no block, showing the alternation from high to low. Diastolic wave *h*; alternation of *v*; alternation of *h*; *a*—*c*=2; ventricular rate 46. No block.

Fig. 5.—In this figure the alternation is clearer, the enlargement being greater. Ventricular rate 46; alternation of *v*; alternation of *h*.

Fig. 6.—Tracing obtained at same sitting as Figure 5, showing apparent alternation of *a* waves. The initial rise following the *v* wave is due to the *h* wave and its level is maintained by the oncoming of the *a* wave, which latter is not visible as an additional rise, hence *a*—*c* cannot be measured. Ventricular rate 46.

In order to attempt an explanation of this alternation it is necessary to stop here to inquire into the manner in which these waves are produced. The wave *v* is explained by Mackenzie[1] in this way: The blood (during ventricular systole) "comes mainly from the periphery into the auricles through the veins. When the auricle becomes filled the surplus distends the superior vena cava and jugular, and hence appears in the tracing as a wave." If we assume this as the correct explanation of the occurrence of the wave, then we must, in order to account for the alternation, assume that in some instances there is a greater surplus distending the vena cava and jugular than in other instances, or at any rate the surplus is sent back or held back with varying force. Since there is no reason to think that the amount of blood flowing from the periphery through the veins to the auricles varies so considerably and so regularly in volume from second to second, we are forced to consider that the cause of the alternation must lie in some condition of the auricular wall. It seems probable that a varying tonicity would permit the auricle to be distended to a varying degree. At times, therefore, the auricle would contain a larger amount of blood than at others, and in consequence there would be a smaller surplus left to distend the vena cava and the jugular. This would make a smaller wave. When the tone of the auricle was greater a smaller amount of blood would be accommodated, a larger surplus would overflow into the vena cava and jugular and a large wave would be caused. The common occurrence of a pulsus alternans in the peripheral circulation presents an analogy which may be used as an argument in favor of the explanation I offer. If there may exist an alternation of the contractility of the ventricle, is it not reasonable to suppose that there may be an alternation of the tonicity of the auricle?

1. Mackenzie: Diseases of the Heart.

We may now turn our attention to the *h* wave and shall find, as I think, that the cause of its alternation lies in the same variability of the auricular tone. This *h* wave was described by Gibson[2] and Hirschfelder[3] (independently) to the inrush of the blood from the auricles into the ventricles after the opening of the auriculoventricular valves, causing the leaflets to be floated up, and bringing about a transient closure of the valves. This explanation is generally accepted. If this is correct, then it is apparent that the condition of the auricular wall will be the chief factor in determining the size of the wave, which will record the influence of this closing of the valves as a wave in the jugular tracing.

The tracing shown in Figure 6 was obtained at the same sitting as that in Figure 4. The plateaus succeeding the *v* waves and preceding the carotid, *c* waves were thought when the tracing was first studied to be due to the auricular contractions. In other words, they were considered to be *a* waves. There was, therefore, apparently an alternating condition of the auricular contracility. This was, however, a faulty intrepretation as we shall see in a moment. Such an alternans action of the auricles has been described by Griffith.[4] It was accompanied by an alternating ventricular contraction. Griffith explains the alternately large and small auricular waves as follows:

> The primary condition is the alternans action of the ventricles. When the systoles are strong they last long enough to prevent the quickly following auricular contraction from driving the blood freely or at all into the ventricles and so a large wave is seen in the jugulars. When the ventricular systoles are weak they do not last so long, and the auricle can drive its blood in larger amount into the ventricle and consequently the jugular wave will be smaller. It is of course only when the *a-c* interval is unduly long, as it was in this case, that alternately large and small auricular waves could be determined in this way by an alternans ventricular action.

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2. Gibson: Lancet, London, Nov. 16, 1907.
3. Hirschfelder: Am. Jour. Med. Sc., September, 1906.
4. Griffith: Quart. Jour. Med., January, 1910.

There was, however, no condition of this sort present in my case. On a closer analysis of the tracing in Figure 6, and in comparing it with the other tracing made at the same time, it became evident that the plateaus already mentioned were due not to the auricular contraction *a*, but to *h* plus *a*. The initial rise of the plateau is due to the *h* wave and its level is maintained by the oncoming of the *a* wave which is not visible as an additional rise.

On two occasions I tried to ascertain the effect of atropin on the block. On both occasions I gave 1/60 of a grain hypodermatically and in both instances there was absolutely no result from its administration. Although the radial pulse was slow, (46), and I had expected to find a block present, this was not the case either time. Hence, I am unable to say what effect atropin would have on the block.

I desire to express my obligation to Prof. George Dock, who first pointed out the alternation of the waves.

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ABSTRACT OF DISCUSSION

ON PAPERS OF DRS. LEMANN AND BECK AND STOKES

DR. HAVEN EMERSON, New York: I have been much interested in result of experimental procedures or distention of the auricles with saline solutions. If one places a dog under ether anesthesia, and floods the auricles quickly with saline solution, the animal will develop auricular paralysis. But if one makes a slow infusion of the saline solution, there will result a condition of auricular vibration (fibrillation). It has been found that by replacing the blood of any tissue by any of the usual artificial circulation ordinary fluids we alter the tone of that tissue, especially the muscular tissue; therefore it is entirely conceivable that by flooding the auricles with saline solution there results an alteration of the *a* wave such as shown by the study just reported. The analysis of heart-block has been explained as being the result of an alteration of the tonicity of the auricular wall. So far as is known, the tonicity of the blood vessels alters but slowly. It must be remembered that the heart muscle has been shown to correspond in every way with the skeletal muscles as regards the output of work and conditions under which work may be done to the best advantage as regards time or load. The heart

muscle, however, does not appear to alter in tone so rapidly as do the skeletal muscles. We should consider the possibility that the tone of the muscle of the heart may alternate nearly as does the tone of the skeletal muscles. Until we can prove consistently that certain procedures alter the tone of the heart muscle we must be conservative in accepting such a change of tone as an explanation of or accompaniment of heart-blocks as instanced in the papers read.

Dr. Albert E. Taussig, St. Louis: I have under observation a case of congenital stenosis of the pulmonic orifice with a patent ductus arteriosus which shows a phenomenon similar to that described by Dr. Lehmann. The patient is a young man, aged 19, a shoemaker. He is able to earn a good living at his work in spite of his cardiac defect. The heart is enlarged and he has the typical murmur and other phenomena characteristic of stenosis of the pulmonic orifice. The *a* wave in the jugular bulb is exaggerated and shows well-marked alternation in height, especially when he is under the influence of digitalis. Tracings taken some weeks ago show that the radial pulse is about normal, while the jugular pulse shows a high *a* wave which alternates in height. This alternation occasionally fails. Another interesting feature of these curves is that at the same time of the alternation of the *a* wave there is an alternation of the *a-c* interval. The higher the *a* wave the longer the *a-c* interval. This is the reverse of what one might expect *a priori*.

AUTOGENOUS VACCINE THERAPY IN ENDOCARDITIS *

E. C. ROSENOW, M. D.
CHICAGO.

The therapeutic value of the injection of dead bacteria in certain localized infections, particularly those of long duration, can no longer be questioned. Their effect in the more generalized infections, particularly in endocarditis, is still very questionable. Wright,[1] Conder,[2] Barr and Bell,[3] report one case each of recovery, while Thompson,[4] reports three recoveries out of a total of seven cases of endocarditis under vaccine treatment. Others have reported a few recoveries. A study of the cases of recovery shows that all were acute infections caused by more or less highly virulent organisms following a definite often severe local infection, and usually developing metastatic abscesses, the cases presenting a picture of pyemia; the type of endocarditis from which every now and then a patient recovers quite independently of the kind of treatment. Horder,[5] Billings,[6] Osler,[7] Libman and others have had uniformly nega-

* From the Memorial Institute for Infectious Diseases. This work was aided by a grant of the American Medical Association and by the Dane Billings Fellowship in Medicine in Rush Medical College, Chicago.

1. Wright: Studies on Immunity, Constable & Co., London, 1909.
2. Conder: Practitioner, August, 1909.
3. Barr and Bell: Lancet, London, Feb. 23, 1907, p. 499.
4. Thompson: Am. Jour. Med. Sc., 1909, new series, cxxxviii, 169.
5. Horder: Quart. Jour. Med., 1909, ii, 289.
6. Billings: Arch. Int. Med., 1909, iv, 409.
7. Osler: Quart. Jour Med.. 1909, ii, 219.

tive results. The cases studied by them were chiefly those which show insidious outset, a prolonged course and which show a progressive anemia and from which organisms with a low grade of virulence are isolated—the type known as chronic septic or infectious endocarditis. In this form of endocarditis all observers report an invariably fatal termination, regardless of the form of treatment employed. All agree that the injection of large doses (200,000,000 and over) do harm. Most observers have noted temporary good effects from the injection of small doses (from 10,000,000 to 100,000,000).

In malignant endocarditis it is obviously difficult to judge, on purely clinical grounds, the effect of the injection of dead bacteria. The series of experiments reported by me recently[8] were undertaken in order to throw more light on the mechanism involved; to determine more accurately the dosage, etc., and to determine why the patient who has an endocarditis of the chronic type in which bacteria of a very low grade of virulence are found dies, while in the more acute infections due to highly virulent organisms, the patient occasionally recovers.

In the first series of experiments it was shown that the injection of dead bacteria always raised the opsonic index when low and increased the leukocytes, but the cases studied went on uninterruptedly to a fatal termination regardless of the increase in leukocytes and opsonic index occasioned by the vaccinations. Very late, however, when the index had dropped far below normal, temporary good effects were noted. It was observed, too, that at times the bacteria behaved very peculiarly toward the patient's own blood. The second series of experiments consists largely of a daily study of the clinical picture and the temperature, the leukocytes, the phagocytic and, what is more important, the

8. Jour. Infect. Dis., Chicago, 1909, vi, 245; 1910, vii, 429, abstr.

destructive power of the patient's blood as compared with normal blood, together with the number of bacteria in the circulating blood.

The more important results brought out by this study may be summarized briefly as follows:

The evidence seems conclusive that the continuation of the infection in chronic infectious endocarditis is due largely to a process of immunization or adaptation of the bacteria to the antibodies of the host. This is shown by the facts (1) that the bacteria grow much more rapidly in the patient's serum than in normal serum; (2) that when grown in the patient's blood or serum both *in vivo* and *in vitro* they acquire a resistance to phagocytosis and a resistance to intraleukocytic destruction; and (3) that they produce alterations in the serum of the patient which robs the leukocytes of something which they need to digest the bacteria when taken up. The destroying power of the patient's blood at these times was found far below that of comparable normal blood. This peculiar behavior of the patient's bacteria and blood was found particularly striking during the time when the number of bacteria are increasing in the circulating blood and for variable periods previous to the occurrence of embolism or arthritis. During the clinical reaction occasioned by a shower of emboli or joint involvement (auto-inoculation) or following the injection of dead bacteria, and especially of normal human serum (which was found to activate the patient's blood *in vitro*) or serum and dead bacteria combined, this peculiar relation of the patient's serum, leukocytes and bacteria disappears, the destructive power of the patient's blood returns and the number of bacteria in the blood shows a corresponding drop. The patient is temporarily improved but weaker than before. The severity of the clinical reaction and the exhaustion of the patient seem to depend (within certain limits) more on the number

of bacteria destroyed in the circulating blood than on the number or size of bacterial emboli (auto-inoculation) or the quantity of serum or dead bacteria injected. Thus on four occasions in one case when the bacterial count was high the injection of 20 c.c. of normal human serum produced a very severe clinical reaction and the number of bacteria showed a marked drop. Transfusion of blood at this time would seem to be dangerous.

The injection of the same amount of serum on fourteen other occasions when the bacteria were at a low point caused no demonstrable clinical reaction and seemed to keep the bacteria at a low point for a period of three weeks. The destroying power of the patient's blood during this time remained up to the normal point. Similar results have been obtained in two other cases. Another striking fact was noted which adds significance to the observations, viz., that often during the time when the bacteria in the blood are on the increase and the destroying power of the patient's blood is below normal the temperature and leukocyte count are lower and the patient seems better. The temperature, however, at once rises when the drop in bacteria begins. In other words, the destruction of bacteria liberates a toxic material which poisons the individual. Hence to combat endocarditis successfully it is necessary to inject, in addition to something which activates the patient's blood, a neutralizing substance which would prevent the intoxication of the already overwhelmed patient. The outlook for a specific serum, however, is very gloomy because the results of animal experiments show that the injection of organisms isolated from chronic infectious endocarditis (which appear to be modified pneumococci) produce an increased susceptibility to subsequent injections instead of an immunity. Moreover, when we bear in mind that in acute malignant endocarditis we are dealing with an overwhelming infection and that in chronic infectious endo-

carditis the reactions produced by vaccination and even by the injection of normal serum in no way differ from those occasioned by embolic processes (auto-inoculation) and that experimental evidence points strongly to a very early and profound alteration in the mechanism of immunity, it would certainly seem that injection of dead bacteria would be of very small therapeutic value if indeed not actually harmful.

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THE IMPORTANCE OF A LOW PROTEIN DIET IN CHRONIC NEPHRITIS

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In planning a diet for chronic nephritis three cardinal principles must determine our selection of food.

First, the amount of protein food must be limited. Since the power of the kidneys to eliminate nitrogenous material is impaired, the amount of such material ingested must be limited to what the kidneys can readily take care of. This necessitates the careful regulation and limitation of the amount of protein food ingested.

Second, a sufficient amount of nutrition must be furnished. Notwithstanding the limitation of protein food, it is essential that sufficient nutriment should be supplied for all needs of the organism. The diet must have a sufficient caloric value, and the loss from limitation of the protein food must be made up by a corresponding increase of the fats and carbohydrates. The caloric value of the diet is of less importance in the more acute stages of acute nephritis, or in acute exacerbations of chronic nephritis. Here, as in all acute diseases, no harm results if the diet for a number of days has a caloric value considerably less than is demanded by the needs of the organism. But in dealing with a chronic condition which may last for months or years, a sufficient number of calories must be furnished or else the body deteriorates from slow starvation.

Third, variety must be provided. No matter how satisfactory a given diet may be, it cannot be strictly

maintained for a long time without the patient becoming so tired of it that he rebels. In a diet for a chronic disease, variety is absolutely essential. It must be provided wisely, or the patient will himself vary his diet, and will probably do so foolishly.

LIMITATIONS OF PROTEIN FOOD

It is safe to say that an average adult in health does not need more than 90 gm. of protein in his food daily. It is known from the investigations of Chittenden and others that a person leading an active life can get along and maintain a condition of health and strength over prolonged periods on about half that amount of protein.

For practical purposes I have taken 90 gm. of protein a day as the maximum for cases of chronic nephritis, above which it is unnecessary to go, and have taken 50 gm. as the minimum, below which it is undesirable to go. These are not absolute limits, for I have had patients in a quiescent stage of chronic interstitial nephritis exceed 90 gm. without apparent injury. On the other hand in some advanced cases the patients have done well on less than 50 gm. of protein in a day over long periods.

Practically, then, in the severer or advanced cases of chronic nephritis we limit the ingestion of protein to 50 gm. daily. In proportion as the case is less severe we allow more protein, taking 90 gm. as the maximum for the slight or inactive stages of the disease.

CALORIC VALUE OF THE DIET

As has been already stated, the diet in a chronic disease must provide a sufficient number of calories to meet the requirements of the system for heat, energy, etc. Roughly speaking, an average adult needs 2,000 calories in twenty-four hours if at rest (as a patient in bed), 2,500 calories for light activity, and 3,000 calories for moderate activity. Three thousand calories may be

taken as the maximum, for in few cases of chronic nephritis are the patients warranted in doing an amount of work that requires more than that.

It will be found practically that individuals differ considerably in their demands in this respect. For example, I have had a number of patients who have been going about and leading a life of light activity, yet maintaining their weight, strength, and general condition of health on 1,500 to 2,000 calories. It is a mistake to force such patients against their inclination to take 2,500 calories or more, simply because it seems to be demanded on theoretical grounds. The maintenance of the weight, strength, and the general condition is a satisfactory practical test of the efficiency of the diet.

Loss of strength and energy and a marked feeling of lassitude are symptoms frequently complained of by these patients. This arises in part from insufficient nutrition, when the patient has a distaste for food, but also in many cases from the ingestion of too much protein in the food. For the waste products of protein metabolism, which the kidneys fail to eliminate, are largely the cause of these sensations and also of the extreme nervousness that is often present. It is extremely gratifying to see these symptoms diminish and disappear when, through the limitation of the protein food, the kidneys can remove the accumulations of waste material of this sort. The loss of appetite also seems to be caused by the excess of this waste material, for with its removal the appetite returns.

We often find patients going through cycles of alternating anorexia and good appetite. It is Nature's attempt to regulate the protein intake. When there is an excess of the waste products from protein food, anorexia ensues and the supply is cut down. When the excess has been removed, the appetite returns, often whetted by the resulting lack of nourishment. But

unless the diet is properly proportioned, an excess of protein is quickly taken, and anorexia again ensues. This process is sometimes exaggerated through the belief on the part of the patient or physician that the feeling of weakness is to be combated by meat, eggs and milk, because of their reputed strength-giving properties.

An increase in the amounts of these foods, relatively rich in protein, simply makes the condition worse instead of better, whereas most gratifying results are often obtained by diminishing the amount of protein ingested, provided sufficient energy is furnished by the other foodstuffs (fats and carbohydrates).

I may allude in passing to the danger in these cases of the fad of the free use of soured milk. If soured milk replaces other protein food, no harm is done. If, because the patient dislikes soured milk, less protein is taken, a distinct benefit may result. But I have seen distinct harm from the addition to a diet already rich in protein of a pint to a pint and a half of soured milk, representing an addition of 20 or 30 gm. of protein a day.

INADVISABILITY OF THE MILK DIET

It was formerly taught that the ideal diet for nephritis, chronic as well as acute, was a strictly milk diet. If other things were allowed in cases of chronic nephritis, it was not because they were considered more desirable, but because it was found practically that the patients would not adhere strictly to this diet for months at a time. Many physicians to-day are trying their best to keep patients with chronic nephritis as close as possible to a strict milk diet. Von Noorden was one of the first to point out a few years ago the fallacy of this line of treatment.

The objection to the exclusive milk diet lies in the fact that, if sufficient nutriment is to be supplied, an excess of protein must be given, whereas the protein

should be diminished in order to spare the kidneys. This is easily demonstrated. Each 100 c.c. of milk contains approximately 4 gm. of protein and furnishes about 70 calories. Let us take 2,100 calories as a convenient number to represent the caloric need of an average patient. As each 100 c.c. furnishes 70 calories, it will require 30 times 100 or 3,000 c.c. to furnish 2,100 calories. In this there will be 30 times 4 gm. of protein, or 120 gm. It has been shown that 90 gm. is the maximum, above which we should not go; therefore, if enough milk is given to furnish a proper amount of nourishment, at least one-third more protein must be given than the maximum amount allowed under the most favorable conditions.

PROTEIN QUOTIENT

It is evident that an article of food is desirable in chronic nephritis according as it furnishes a large number of calories, and yet contains a small number of grams of protein, provided, of course, that it is easily digested and assimilated, and is acceptable to the patient.

I have found it convenient to classify the foods containing protein on this principle. I have used the word "protein quotient" to represent the number of calories furnished by a food for every gram of protein it contains. The protein quotient is the quotient obtained by dividing the calories furnished in a given amount by the number of grams of protein it contains. For example, since 100 c.c. of milk contain 4 gm. of protein and furnish 70 calories, therefore the protein quotient for milk is 70 divided by 4, or 17½, indicating that 17½ calories are obtained for every gram of protein in milk.

We may speak of the protein quotient of a diet. For example, if a diet contains only 50 gm. of protein yet furnishes 2,000 calories, its protein quotient is 40. Or if 90 gm. of protein is allowed for 2,000 calories the protein quotient would be 22 2/9. In chronic nephritis,

then, the protein quotient will range from 22 to 40, and the more severe the case the higher should the protein quotient be.

Table 1 gives a list of the common articles of food arranged according to their protein quotients.

TABLE 1.—COMMON ARTICLES OF FOOD ARRANGED ACCORDING TO THEIR PROTEIN QUOTIENT

Cream (30%)	85.7	Fat ham	33⅓
Bacon	60.0	Mutton and pork	23⅓
Cake	58.0	Custard	20.0
Cream (20%)	57.0	Baked beans	18.0
Mashed potato	55.0	MILK	17½
Rice (boiled)	50.0	Soup (puree)	16⅔
Chocolate	46.0	Butter beans	16.0
Potato	45.0	Cheese (full cream)	16.0
Pudding (simple)	44.0	Lima beans	15.0
Zwieback	40.0	Green peas	14.0
Crackers	39.0	Buttermilk	13⅓
Shredded Wheat	35.0	"PROTEID PORTION"	12½
Parsnips	35.0	Fat meat	12.5
"CEREAL PORTION"	35.0	Egg	11.5
Green corn	33⅓	Scrambled egg	11.5
Cereal (cooked)	30.0	Fish chowder	11.0
Macaroni (cooked)	30.0	Oysters	8⅓
Bread	28.0	Lean meat	6.0
Gruel (milk)	25.0	Fish	6.0
Cocoa	25.0	Lobster	5.0
Beets, carrots	25.0	Beef juice	5.0
Onions, squash	25.0	White of egg	4.0
"Vegetables"	20.0		

TABLE 2.—COMMON ARTICLES CONTAINING NO PROTEIN

One Hundred Grams of Food.	P.	F.	C.	Cal.	Common Measures.	P.	F.	C.	Cal.
Butter	..	85	...	800	Pat (⅓ oz.)	..	9	..	80
Olive oil	..	100	...	900	Tablespoon	..	15	..	125
Sugar	..	...	100	400	Teaspoon	..	..	6	25
Sweet fruits	..	...	10	40	One-fourth lb.	..	..	12	50

THE NEED OF DIET CHARTS OR TABLES

It is evident that, if these principles are to be applied in arranging the diet of a patient, certain data must be at hand in reference to the composition of different foods and their caloric value. Without these data, scientific regulation of the diet is impossible. This information may be obtained from Atwater and Bryant's tables,[1] or from tables now published in many books on dietetics and in some books on treatment. I presented to the pro-

1. The Chemical Composition of American Food Materials, Bull. 28, U. S. Dept. Agric. Off. exper. stations, Wash. (Revised edition).

fession a year ago a convenient diet chart,[2] which contained the statistics for the common articles of food, together with a brief summary of the principles of dietetics. The values given in this chart are approximate only, but are sufficiently accurate for practical use. They are taken as the basis of calculations in this paper. The chief value of the chart is its convenience. With such tables a diet containing the proper amount of protein and at the same time furnishing the desired number of calories can be constructed.

VARIETY, PROTEID PORTIONS, CEREAL PORTIONS

It was found that the third requirement was variety, in a diet that is to continue for a long period. The problem is to furnish variety and a sufficient amount of nutriment, and yet to regulate the amount of protein and prevent it from exceeding a given amount.

If the percentage of protein in different articles of food is known, it can easily be calculated what amount of each article will furnish a given quantity of protein. From our present point of view, these various amounts of the different articles may be regarded as equivalent one to another, and may be substituted for each other. I have designated these equivalent amounts of food as "portions." For example, milk contains 4 per cent. of protein, eggs 13 per cent., and meat 20 per cent. Therefore 100 gm. of milk would furnish 4 gm. of protein, the same amount of egg 13 gm., and of meat 20 gm. One egg weighs on the average 2 ounces, or 60 gm. Therefore it will contain approximately 8 gm. of protein. It would require 200 gm. (or c.c.) of milk to furnish 8 gm. of protein, but the same amount would be supplied by 40 gm. of meat. Therefore one egg may be regarded as equivalent to 200 c.c. of milk or 40 gm. of meat, and each of these amounts is one "portion." These albumi-

2. A Practical Diet Chart, Massachusetts Med. Soc., 1909; Boston Med. and Surg. Jour., Sept. 30, 1909, p. 457. Note: These diet charts are now published by W. B. Saunders Co.

TABLE 3.—PROTEID PORTIONS

Under this head are included the common articles of food that are relatively rich in protein. Each "portion" contains 8 grams of protein—the amount in one egg. Therefore, in calculating the amount of protein in a diet, one portion is equivalent to another. Variety may be secured by substituting one portion for another which has been ordered in a diet.

Each of the following amounts constitutes one proteid portion:

P.	F.	C.	Cal.		
8	5.5	....	80	Egg.	One.
8	8.0	8.0	140	Milk.	One "glass" (200 c.c.). (A tumbler or coffee cup 4/5 full.)
8	1.5	13.0	100	Buttermilk.	One-half pint. (A tumbler or coffee cup *full.*)
8	2.0 to 8.0	.... to	50 to 100	Meat or fish.	One and one-third oz. (40 grams). One oz. is the amount of meat in the lean part of a lamb chop; or 1 cubic inch of meat or fish. If steak or fish is 1/2 inch thick, surface would be 2x1 inches.
		Varies with amount of fat.			
8	10.0	1.0	120	Cheese.	One oz. (30 grams).
8	6.0	1.0	90	Scrambled egg, or omelette.	One and one-third tablespoons (80 grams).
8	3.0	8.0	90	Fish chowder.	One hundred grams (3 1/3 oz.).
8	5.0	13.0	130	Puree soup.	One-half pint.
8	7.0	16.0	160	Custard.	Four and one-half oz. (a small cup) (130 grams).
8	19.0	29.0	320	Ice cream	Five oz., a small cup, or rather large serving (160 grams).
8	2.0	3.5	65	Oysters.	Eight average-sized (each weighing 10 grams, or 1/3 oz.). (One oyster of this size contains 1 gm. protein.)
				Clams.	Same as oysters, according to size.
8	5.0	5.0	100	Average proteid portion (P. P.).	

noid substances, known as proteids, and other similar articles which are relatively rich in protein are conveniently grouped together. Portions in this group are designated as "Proteid Portions," and the unit is 8 gm. of protein, the amount of protein in one egg.

In a similar way bread contains on the average 9 per cent. of protein, boiled rice 2 per cent., and cooked cereals 2 per cent. It is found that an average slice of bread weighs about 40 gm. and contains about 4 gm. of protein. Two hundred gm. of boiled rice or cooked cereal would furnish the same amount. A number of the staple articles of food are grouped together on this basis of 4 gm. of protein to each portion, and for convenience these are called "Cereal Portions." Each cereal portion, containing 4 gm. of protein, contains half as much protein as the proteid portion, which has 8 gm.

Table 3 gives a list of proteid portions, and Table 4 gives a list of cereal portions. In these two tables are included all the more common articles of a mixed diet, and from them sufficient variety may be obtained to satisfy any reasonable person.

The regulation of the amount of protein ingested is easy by means of these portions. We can order a certain number of proteid portions (P.P.) and a certain number of cereal portions (C.P.) and know with sufficient accuracy just how much protein the patient gets, although he may be given free choice of all the articles in these lists. For example, if it is desired to give the patient 60 gm. of protein in a day, 4 P.P. ($4 \times 8 = 32$) and 7 C.P. ($7 \times 4 = 28$) can be ordered; or 5 P.P. ($5 \times 8 = 40$) and 5 C.P. ($5 \times 4 = 20$). If the patient is ordered 5 P.P., he might take 2 eggs, one glass of milk, and 2 lamb chops; or one egg, one portion (40 gm.) of fish, 80 gm. of meat, and a cup of custard; or any other combination to make up 5 P.P.; yet from these 5 P.P. he will always get 40 gm. of protein. From the 5 C.P. he will get 20 gm., and the total will always be 60 gm., whatever the combination.

TABLE 4.—CEREAL PORTIONS

The articles of food in this table are less rich in protein than those included under the head of proteid portions, but they are staple articles of food and a considerable part of the protein of the food is derived from them. The amount of protein in each cereal portion is 4 grams—the amount is a fairly thick slice of bread. Thus a cereal portion contains half as much protein as a proteid portion. Calculations and substitutes may be made in the same way as with proteid portions.

Each of the following amounts constitutes one cereal portion:

P.	F.	C.	Cal.				
4.0	0.5	24	115	Bread.	One and one-third oz. (40 grams). One slice of an average-sized loaf; 1 tea roll; ½ breakfast roll; 1 muffin.		
4.0	6.0	40	230	Cake.	Average piece 2 oz. (60 grams).		
4.5	4.0	28	165	Crackers.	One and one-third oz. (40 grams). (Weigh different kinds.)		
3.0	0.5	22	100	Shredded Wheat.	One biscuit.		
4.0	5.0	30	175	Pudding.	Simple puddings (bread, rice, Indian, tapioca, cornstarch), one serving, 3½ oz. (100 grams).		
4.0	10.0	38	250	Pie.	Average piece (100 grams).		
4.0	....	40	180	Potato.	Two moderate-sized, 200 grams, 1 potato = ½ C. P.		
4.0	6.0	36	220	Mashed potato.	3 tablespoons.	200 grams.	1 tablespoon = ⅓ C. P.
4.0	....	12	60	Butter beans.	2 tablespoons.	40 grams.	1 tablespoon = ½ C. P.
4.0	....	11	60	Lima beans.	2 tablespoons.	50 grams.	1 tablespoon = ½ C. P.
4.0	....	10	60	Peas.	2 tablespoons.	60 grams.	1 tablespoon = ½ C. P.
4.0	....	27	125	Green corn.	3 tablespoons.	140 grams.	1 tablespoon = ⅓ C. P.
4.0	1.0	24	120	Cereal (cooked).	4 tablespoons.	200 grams.	1 tablespoon = ¼ C. P.
4.0	1.0	33	160	Corn Flakes, etc. (dry cereals).	8 tablespoons.	40 grams.	1 tablespoon = ⅛ C. P.
4.0	....	48	200	Rice (boiled).	4 tablespoons.	200 grams.	1 tablespoon = ¼ C. P.
4.0	2.0	21	120	Macaroni.	4 tablespoons.	140 grams.	1 tablespoon = ¼ C. P.
4.0	2.0	21	120	Vermicelli.	4 tablespoons.	140 grams.	1 tablespoon = ¼ C. P.
4.0	....	30	140	Parsnips.	4 tablespoons.	200 grams.	1 tablespoon = ¼ C. P.
4.0	....	20	100	Carrots.	4 tablespoons.	200 grams.	1 tablespoon = ¼ C. P.
4.0	....	20	100	Squash.	4 tablespoons.	200 grams.	1 tablespoon = ¼ C. P.
4.0	....	20	100	Turnips.	4 tablespoons.	200 grams.	1 tablespoon = ¼ C. P.
4.0	....	20	100	Onions.	4 tablespoons.	200 grams.	1 tablespoon = ¼ C. P.
4.0	1.0	30	140	Average cereal portion (C. P.).			

Variety and the regulation of the amount of protein, having thus been provided for, it must next be considered how this scheme affects the problem of the amount of nutrition—the total calories for the day. For, although each portion contains the same amount of protein, the number of calories varies considerably. For example, 1 P.P. of lean meat furnishes only 50 calories, while 1 P.P. of ice-cream furnishes 320 calories; or 1 C.P. of butter beans furnishes 60 calories, while 1 C.P. of cake gives 230 calories. These seem wide variations, but when a person is changing the diet rather frequently he comes pretty near the average figures given in the tables. Sufficient accuracy will therefore be attained by counting each proteid portion as 100 calories and each cereal portion as 140 calories.

THE METHOD OF PLANNING A DIET

The number of grams of protein that the patient should have must first be determined according to the severity of the case. Then the number of calories the diet should furnish must be decided. This is determined by a consideration of the normal weight of the patient and the amount of his activity.

An adult requires in twenty-four hours:

At rest .....14—16 calories per pound of normal weight.
At light work.....16—18 calories per pound of normal weight.
At moderate work.18—20 calories per pound of normal weight.

Roughly stated, an average-sized man requires:

At rest ..... 2,000 calories in 24 hours.
At light work ..... 2,500 calories in 24 hours.
At moderate work ..... 3,000 calories in 24 hours.

Let us suppose, for example, that it is desired to prescribe a diet which contains 70 gm. of protein and furnishes 2,000 calories. It is desirable to prescribe a certain amount of cream in such a diet, both because it is an acceptable article of food and because of its high caloric value and relatively low amount of protein.

	P.	F.	C.	Cal.
Cream, 20 per cent., 1 oz.	1	6	1	60.
Cream, 30 per cent., 1 oz.	1	9	1	90.

Each ounce of cream contains 1 gm. of protein. A patient can readily take from 2 to 6 or 8 ounces of cream daily.

In planning a diet for a given number of grams of protein, the first number lower that is divisible by four is selected. This number of grams, being a multiple of four, can be provided for from the proteid portions and cereal portions. The number of grams above this is furnished by cream, each ounce of cream furnishing 1 gm. All the protein has now been provided for and no more can be added. The number of calories which have already been furnished are calculated and then the balance is provided for by articles which do not contain protein, such as butter, sugar, fruit, etc. These articles and their composition and caloric values are given in Table 2.

For example, it is desired to get 2,000 calories from a diet containing only 70 gm. of protein. The first number below 70 that is divisible by 4 is 68. Therefore 2 ounces of cream are ordered and the remaining 68 gm. are divided among the proteid and the cereal portions. If 5 P.P. is tried, that furnishes 5 times 8 or 40 gm. of protein, and there are 28 gm. left, which would be provided for by 7 C.P. Now 5 P.P. furnish on the average 500 calories, 7 C.P. furnish 980 calories, and 2 ounces of 20 per cent. cream furnish 120 calories. This provides for 1,600 calories. Since 2,000 calories are wanted and no more protein can be given, 400 calories must be obtained from non-protein foods. One ounce of butter would furnish 240 calories, 250 gm. (half a pound) of sweet fruit would give 100 calories, and 3 teaspoonfuls of sugar would give 75 calories. The total is 415 calories, or 15 calories more than is needed. It is not difficult to calculate such a diet.

This diet is tabulated in Table 5:

TABLE 5.—DIET FURNISHING 2,000 CALORIES WITH 70 GRAMS PROTEIN

	P.	F.	C.	Cal.
5 P.P.	40	25	25	500
7 C.P.	28	7	210	980
Cream, 20%, 2 oz.	2	12	2	120
Butter, 1 oz.	..	27	...	240
Sweet fruits, 250 gm.	..	..	25	100
Sugar, 3 teaspoonfuls	..	..	18	75
Total	70	71	280	2015

The diet may be varied further by the addition of any of the so-called "fodder-vegetables," which include asparagus, string beans, Brussels sprouts, cabbage, cauliflower, celery, cucumbers, greens, lettuce, pumpkin, radish, rhubarb, spinach and tomatoes. These do not in themselves furnish enough protein or nourishment to count. They are, however, acceptable to the taste, they add to the volume of the meal, and they offer a ready method of introducing butter or oil in the diet. They may be taken in such amounts and variety as are desired, provided they are easily digested.

This diet may be reduced to ordinary terms for the patient as follows:

Breakfast.—Fruit, 125 gm. (one-half of a large orange). Cereal, 4 tablespoons (1 c.p.), with 1½ ounces of cream and 1 teaspoonful of sugar. One egg (1 p.p.) on 1 slice of toast (1 c.p.) with 1 pat (⅓ oz.) butter. Coffee, with ½ ounce cream and 1 teaspoonful sugar.

Lunch.—Scrambled egg, 80 gm., 1⅓ tablespoons (1 p.p.). Toast, 1 slice (1c.p.) with 1 pat butter. Cake, 60 gm., average piece (1 c.p.). Fruit, 125 gm.

Dinner.—Oysters, 4 average-sized (½ p.p.). Puree soup, 4 ounces (½ p.p.). Fish, 40 gm. (1 p.p.). Meat, 40 gm. (1 p.p.). Bread, 1 slice (1 c.p.), butter, 1 pat. Potato, 1 moderate-sized (½ c.p.). Boiled rice, 2 tablespoons (½ c.p.). Spinach (or other fodder vegetables). Pudding, 100 gm., 1 serving (1 c.p.). Coffee, demi-tasse, with 1 teaspoonful of sugar.

With such a diet planned, the patient is instructed that wherever a proteid portion or a cereal portion is indicated, any other equivalent portion from the list

may be substituted. Moreover, if at one meal he does not care for the full allowance, any article omitted or its equivalent may be taken at another meal. The patient may, if he desires, take more fruit, butter, sugar, or other non-protein food than is ordered.

Such a menu gives a patient a diet that is sufficient in amount and nutritive value, is satisfactory in variety to most people, is easy to obtain at an ordinary home table or at a hotel, and can be varied by the patient to suit his taste; and yet with all the changes the patient is getting a well-balanced ration and his protein intake is strictly regulated.

I find that patients are able to understand these regulations without much difficulty, although the patient should be kept under rather close supervision until the ideas are thoroughly understood. Later the patient should make a report at stated intervals as to just what he has taken in twenty-four hours. In this way a case may be followed and controlled indefinitely.

Where accuracy is important the food should be actually weighed. It is a good plan to do this at the start in any important case. After weighing the different kinds of food for a time the portions can be estimated with sufficient accuracy by the eye. For the purpose of weighing food at the table I have found the food scales designed by Dr. Hart extremely satisfactory.[3]

RESULTS

What can be accomplished by such regulation of the diet?

Much will depend on the stage of advancement of the disease and on its activity. The treatment is prophylactic and palliative rather than curative. Naturally the best results are obtained in cases in which the functions of the kidneys are but little impaired, in the early or inactive stages of the disease. But surprisingly good

3. Hart, T. S.: A New Food Scale, THE JOURNAL A. M. A., Aug. 7, 1909, p. 457.

results have been obtained in some cases of cardiorenal disease, so advanced that we should ordinarily despair of helping them.

When the protein metabolism can be adjusted relief from those symptoms which are due to failure to eliminate these waste products is obtained, and a condition of relative health is restored. The relief from nervous symptoms, anorexia, and the feeling of lassitude or fatigue has already been mentioned. Perhaps the most gratifying result, however, is the lowering of blood-pressure and the consequent relief of the burden thrown on the heart. It would appear that the increased blood-pressure in case of chronic nephritis is due, in part at least, to the excess of these waste products in the body. Such a reduction of blood-pressure cannot be secured in every case, but a gratifying reduction occurs in a large majority, and a surprising drop in many. Blood-pressures ranging from 200 to 180 mm. are commonly reduced below 160, not infrequently to 150 or 140.

One of my patients over 60 years old, starting with a blood-pressure of 190, finally reached and maintained for months a pressure ranging from 120 to 130. He enjoyed better health and strength than at any time since the symptoms arose two years before, but he died recently from an intercurrent disease, being unable to resist successfully an acute infection which resulted in pleurisy and pericarditis. I am confident that his life by regulation of the diet was prolonged fully two years longer than it would have been otherwise. I can see no reason why he should not have lived for an indefinite period longer but for this intercurrent affection.

Another patient was taken in charge a year and a half ago, after the second severe attack of uremic convulsions occurring within three months. He has been free from uremic attacks since then; he is in better health than for a number of years, and his blood-pressure for the past year has shown an average of 160, although it was 210 when treatment began.

In another case of advanced interstitial nephritis with failing cardiac compensation the blood-pressure was reduced from 260 to 180, although the patient had had symptoms for two years and marked symptoms for several months. In this case, however, the improvement lasted but two months, although during that time the patient was practically free from symptoms. Then the former symptoms recurred, with an increase of blood-pressure, so that in two months more it had again reached 260. The patient lived only about two months after that. Surely this was a very advanced case, yet great relief ensued for a time.

Such results cannot be secured in all cases, of course; nevertheless, they are exceptional rather in the degree of reduction of blood-pressure than in the fact that a satisfactory result was obtained. I have had a good result now in so many cases in which I hardly dared hope for it, that I am beginning to predict relief in almost every case. Contrast such results with the transient and unsatisfactory results of drug treatment, and I think you will agree that it is well worth while to take the moderate amount of trouble involved in the proper regulation of the diet.

The stumbling-block in the past has not been the absence of sufficient knowledge, for the scientific laboratory workers have known the underlying facts for years, but the difficulty of getting that knowledge into a form simple enough to enable the physician to apply it in every-day practice. This difficulty is overcome, at least in large measure, by the charts and tables here mentioned.

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ABSTRACT OF DISCUSSION

Dr. G. C. Smith, Boston: I have been interested during the past fifteen years in dietetics in chronic diseases, and the best methods of dealing with chronic affections. There are so few remedies in the way of drugs that can be continued with benefit for a long time, that it is necessary to get at these

troubles in some other way, and the dietetic way seems to be the one indicated. The first instruction in New England given on the subject of dietetics has been given by Dr. Arnold. It is really a misfortune that every institution teaching medicine in this country does not have a definite chair of dietetics. It seems to me that this is too large a subject for a man who is teaching another subject to give instruction on. For the past two or three years, however, there has been an improvement in the manner in which the young physician in New England handles the chronic cases, dietetically speaking. Our experience has been somewhat different from Dr. Arnold's in some respects. The question of calories which enters into any diet can be modified very much, as explained by Dr. Arnold in his tables. In other words, in the cases that are primarily renal, the patients as a rule are very thin, usually cold and anemic. In such patients, the carbohydrates and fats must predominate in the diet. On the other hand, in the cardiorenal cases we often find the reverse. In these cases frequently the cardiac part is primary and the interstitial changes or process in the liver, the kidneys and elsewhere are secondary and consequent upon the prolonged congestion of these organs. Such a prolonged congestion, with the long duration of the disease, produces changes in metabolism which weaken the patient, making him take much less nourishment because he suffers with indigestion. The nourishment too may be of the wrong kind, *e. g.:* One may cut out the proteid and increase the "pap," and especially the sweets and bread with their high percentage of starches. By doing this and adding cream and butter the calories are much increased. Such patients are unable to take much exercise because of the cardiorenal disease; therefore, they remain in the house and at rest. A reduction in the number of calories in such cases should be made by reducing the amount of fat and carbohydrates. Then the question of the proteid element comes up. There is no doubt in this class of cases but that the proteid element must be higher than seventy grams; one cannot produce an improvement in metabolism without more proteid; hence we must give it to furnish the best nutrition for the cells of the body. Consequently in all these cardiorenal cases it will be found advisable to raise the amount of proteids higher than physicians as a rule recommend. This may be considered a little off from the subject of the paper, but it is such a common thing to find the renal and cardiac cases mixed that I believe it is well to consider them. Another thing which should be considered is the different manner in which the number of calories can be made up from the diet lists.

Dr. Philip S. Roy, Washington, D. C.: I have used Dr. Arnold's charts regularly. As to the question of fats and carbohydrates overloading the system and the metabolism becoming deranged as a consequence thereof, as mentioned by Dr. Smith,

I have not found that the case if Dr. Arnold's plan be followed. When one wishes to lessen the number of carbohydrate calories, he can replace these calories with fat. Three pints of milk with a pint of cream and one ounce of butter equals about 2,000 calories. This will give all the energy needed. I am in accord with the statement that the proteids in disease of the kidney should not be above 50 grams daily.

Dr. H. D. Arnold, Boston: I am glad that Dr. Smith mentioned the cardiorenal cases in which the cardiac end predominates. The problem here is somewhat different, in that the power of the kidneys to eliminate nitrogenous material is less seriously impaired. Greater liberality in the use of protein food may be allowed, yet even in these cases there is no necessity for large amounts. I think that 50 grams of protein are enough for the purposes of tissue building, including the heart. It is of great importance that there should be an abundant amount of nutrition—a sufficiently high caloric value to the diet—but beyond the amount of protein needed for tissue-building, this nutriment is just as well, if not better, derived from the other foodstuffs. Often, however, our plan must be modified because of questions of digestion and assimilation. Some people cannot digest fats well, and others have difficulty with the carbohydrates. I would not be understood as maintaining that we must always give the number of calories which are indicated by theoretical calculations. Often we find a patient will maintain weight and strength, and may even gain, on 1,500 calories when 2,000 or more are demanded theoretically. If such is the case it is a mistake to force the patient to take the larger amount.

The only credit I feel that I am entitled to in this work is in getting our knowledge in dietetics into a simple, practical form for application in ordinary practice. There is nothing in it that is new or that has not been utilized by the laboratory workers in metabolism experiments for years. But the data have been too complicated for use in ordinary cases and have not been easily available. If we can apply these principles to ordinary patients we shall plan diets with far more intelligence than we have done in the past.

INFLUENCE OF PERIGASTRIC LESIONS ON GASTRIC SECRETIONS

STUDY BASED ON CLINICAL AND EXPERIMENTAL OBSERVATIONS

M. J. LICHTY, M.D.
CLEVELAND

A few years ago I was impressed with the extraordinary frequency with which I met patients who had gastric hyperacidity with their gastric symptoms. Many of them were of a neurotic type and could possibly have been diagnosed and dismissed as cases of nervous dyspepsia with hyperacidity. But a great many others, eventually and often surprisingly, gave positive symptoms and physical signs pointing to disease of other organs near the stomach, which, no doubt, influenced the gastric secretions and made the diagnosis of nervous dyspepsia unwarranted. In a discussion of this matter with my brother, Dr. J. A. Lichty, of Pittsburg, I found that he had the same experience. On account of the belief that the very frequent diagnosis of dyspepsia with hyperacidity was often unwarranted, we decided to investigate the subject more minutely, both from clinical observations and by experiments on animals.

SUMMARY OF CLINICAL OBSERVATIONS

In a review of the cases of 600 patients who consulted me in private practice, who complained of symptoms referring to the stomach, and on whom gastric analyses were made, 318, or more than 50 per cent., had a gastric juice which was hyperacid. The number of cases with normal acidity, subacidity and achylia gastrica

was less than those of gastric hyperacidity. This excessive acidity could be accounted for in several ways. Some were cases of simple nervous dyspepsia with hyperacidity. Many could safely be diagnosed as catarrh of the stomach with hyperacdity. A considerable number of patients had ulcer of the stomach. But others had a hyperacidity which, from what the clinical and experimental work now lead me to believe, was secondary to lesions of the digestive tract in organs surrounding the stomach.

I regret that my own tabulated report of very positive diagnoses of appendicitis and gall-bladder disease is so limited. It may be worthy of mention, however, that, in 54 per cent. of the fifty-six cases of acute and chronic appendicitis seen the last few years in private practice, examinations, including gastric analyses, were made. And, of the cases in which these gastric analyses were made, 83 per cent. showed a hyperacidity. In nearly all of the cases diagnosed as appendicitis the advice for operation was warranted, but only 65 per cent. of these cases were treated surgically, three-fourths of which had gastric analyses which showed a hyperacidity in 75 per cent. of the analyses. It appears, therefore, that of the patients operated on, as well as in those not operated on, more than 75 per cent. had a gastric hyperacidity.

In a still more limited number of gall-bladder cases (forty in all), 75 per cent. showed a gastric hyperacidity and, of those gall-bladder cases in which the diagnosis was verified by operations, more than 50 per cent. had a gastric hyperacidity. Those gall-bladder cases studied at operation which showed no hyperacidity were peculiarly interesting, inasmuch as they quite universally showed a gastric secretion with the very opposite extreme, a marked hypo-acidity. This hypo-acidity was usually present when the patient's physical condition had been greatly reduced by prolonged illness, or by extensive adhesions which bound together both stomach and gall-bladder, interfering directly with the motor

power of the stomach. Two of the operative gall-bladder cases with subacidity had most striking gastric symptoms. The gastric analysis showed a marked deficiency of acids, the presence of lactic acid, as well as occult blood in several repeated analyses, making one very suspicious of gastric carcinoma. But the operations in these two cases showed nothing but gall-stones, and a perfectly healthy stomach except for adhesions to it. Another gall-stone case, with hypo-acidity and a secondary anemia, so marked that the diagnosis of some form of serious primary anemia was considered, had most dense adhesions between the gall-bladder and stomach, as well as an old perforation of the gall-bladder, which allowed the escape of several small stones into the peritoneal cavity. These stones, however, had been held adjacent to the gall-bladder by the firm adhesions.

Reference must here be made to the very striking similarity of figures and percentages in a study of a greater number of cases taken from the records of Dr. J. A. Lichty. Gastric analyses performed in 111 out of 258 of his cases of appendicitis showed a hyperacidity in 64 per cent. of the analyses. Of his 127 patients subjected to operation only forty-nine had had a gastric analysis, but in 69 per cent. of the cases a gastric hyperacidity was present, showing, therefore, a hyperacidity in two-thirds of all appendicitis patients so examined, whether operated on or not operated on. In 157 of 250 gall-bladder cases, which he tabulated, gastric analyses showed a hyperacidity in 54 per cent. of analyses; and, in those gall-bladder cases treated surgically in which gastric analysis had been made, 53 per cent. had an excess of gastric acidity.

Similar study of the gastric juice has been made recently by others:

Graham,[1] in his work with the Mayos, has very recently referred to the gastric symptoms arising from surgical

1. Graham, C., and Guthrie, D.: The Dyspeptic Type of Chronic Appendicitis, THE JOURNAL A. M. A., March 19, 1910, p. 960.

conditions of other abdominal organs, though it was not his experience to notice this frequency of gastric hyperacidity.

Paterson,[2] of London, only a few months ago, expressed his surprise at the frequency of gastric symptoms and the change in gastric secretions caused by appendicitis. In his opinion, the many symptoms of gastric ulcer and even gastric hemorrhage were found at times, by study as well as at operation, to be the sequel of appendicitis. In a few of his cases there was a normal acidity, in about 30 per cent. a hypo-acidity, and in the remaining a marked hyperchlorhydria. He says that "a combination of marked symptoms of gastric ulcer with a negative gastric analysis is suggestive of chronic appendicular disease," and that "in recent years it is becoming gradually recognized that hematemesis, accompanied by pain and vomiting, is not pathognomonic of gastric ulcer." His statement that a gastro-enterostomy will not remove a diseased appendix is strikingly significant. While my experience is not exactly parallel with that of Paterson, since mine shows appendicitis frequently with a positive change in gastric secretion instead of a negative gastric analysis, as he states, yet I am very happy to refer to his comment of associated symptoms.

Here I wish to refer to a patient of my own who, three years ago, had a gastro-enterostomy for a gastric ulcer, which was nearly perforated and was excised at operation. Another ulcer was found to be present at the same time. The operation was done hurriedly. The patient made only a fair recovery and required an entero-enterostomy a year later to correct a vicious circle. Previous to the first, and following the second operation, the patient's gastric secretions were high, but within the last year she again developed vomiting and there was occasional blood in the vomitus. The tenderness over

2. Paterson: Appendicular Gastralgia in Appendicitis as a Cause of Gastric Sypmtoms, Lancet, London March 12, 1910.

the appendix, which had been noticed the last few years, became more marked and the appendix was removed from dense adhesions only a few months ago. At present the patient seems to be making a good recovery.

W. S. Fenwick[3] calls attention to a mild type of hypersecretion, the result of latent disease of the appendix. He says:

> As a rule, it displays an intermittent character for several years and each fresh addition is ascribed by the patient to a chill, mental anxiety, or some indiscretion of diet. Considerable time after it has attained the chronic stage, the typical symptoms of a moderate hypersecretion continue to manifest themselves, but, with the progress of time, paroxysmal pain is gradually replaced by discomfort and distention, which persists during the day, the symptoms varying to a great extent according to the appendicular lesion and the concomitant state of the gastric secretion.

Moynihan[4] states, that, in his view, "the typical gastric ulcer in the medical text-book is frequently the appendix." In his study, recently published he considered the pathology and symptoms of the associated lesions of the appendix and stomach without giving much attention to the gastric secretions. I myself believe that the typical chronic dyspepsia (of the medical text-book) with change of gastric secretions is frequently the appendix or the gall-bladder.

EXPERIMENTAL OBSERVATIONS

A summary of earlier clinical observations, as well as those of others more recently made, has fully justified an investigation of this subject from an experimental basis. Experiments on a number of dogs were begun two years ago and have been continued constantly since, with some very satisfactory and surprising results. The method of experimentation, briefly described, was as follows:

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3. Fenwick, W. S.: Lancet, London, March 12, 1910.
4. Moynihan: Brit. Med. Jour., Jan. 29, 1910.

A number of healthy dogs were secured and a study was made of their gastric secretions. At definite intervals of two or three days the dogs were not fed until noon; then a meal of about 8 ounces of water, containing bread sufficient in quantity to make a gruel, was inserted into the stomach with a bulb and a stomach-tube. Thirty minutes later, this meal was removed and analyzed. We soon found that, if the bread and water remained in the stomach much longer than thirty minutes, the stomach was empty and the secretions and acids were low. In other words, the gastric secretions in dogs supplied with practically the Ewald meal were at the highest about thirty minutes after feeding. After a dozen or more test meals were given to each dog, and a fairly accurate average estimation could be made of the gastric secretion, these dogs were subjected to laparotomy. At the first operations the gall-bladder was opened and filled with cinders and pebbles. Then, again, about a dozen or more analyses were made. After that period, the dogs were operated on a second time, at which time the appendix was opened and filled with foreign bodies, which were fixed there with sutures. The appendix in the dog is, of course, rather a diverticulum of the cecum than a real appendix as in man. After the operation on the appendix, a third series of gastric analyses was made. Following these operations and analyses, if death had not occurred, a third laparotomy was performed, or the animal was bled to death in some other experiment and a post-mortem examination was made to see what pathologic conditions had been caused by the former operations. Out of a number of dogs secured for these experiments, only seven survived all this analytical work and all these surgical operations.

The information which we have gained from these surgical operations, fifteen in all, and from the gastric analyses, exceeding 500 in number, is in our estimation worthy of consideration. Though only seven dogs were kept for any length of time, and subjected to operations

with gastric analyses before and after, several dogs were kept under observation and subjected to analysis only. We soon found that the study of these numerous test meals was of no value or constancy, unless done with much caution and care. Even then, there was considerable variation in the gastric acidity, which indeed was the only secretion studied, including free hydrochloric acid, combined hydrochloric and total acidity.

When the dogs were given the Ewald meal at noon, as previously described, and then fed again with meat and other food soon after the Ewald meal was removed, but not any oftener that day, there was a fairly constant acidity. If, however, the dogs were fed oftener and excessively the remainder of the day, the following day the acids were higher, even though the test meal given at noon was the first food of that day. On the contrary, we also noticed that, when the dogs were starved for forty-eight hours and then given the test meal, the acidity was constantly and markedly very much lower. This notice of a hypo-acidity after hunger or starvation came in a peculiar way. At one time daily analyses were begun on six new, healthy dogs. After several analyses were made on each one it was suddenly noticed that on alternate days the acids were high one day and very low the next. The variation was so great and constant that the physicians who made all the analyses could not overlook or explain it, until they found that, by some misunderstanding of the man who fed the dogs, the animals were given food after the removal of the test meal only every second day. They were then very hungry and ate much. The day following such a full meal the acids were generally high, but the second day thereafter, without any food for forty-eight hours, they were just as constantly low. At another time we secured several new dogs, on which gastric analyses were impossible or of little value, except for one point, the influence of excitement on the secretion. While most of the dogs usually took the stomach-tube and test meal with-

out any difficulty, these dogs fought such a procedure stubbornly. Very rarely could we recover a meal from these dogs. If taken at all, it had to be taken promptly at the end of half an hour; then it was very acid. Sometimes the animal fought the introduction of the tube and meal so stubbornly that vomiting and diarrhea immediately followed. These dogs were not kept long, though long enough to make us believe that excitement caused increased acidity and peristalsis.

A summary of the analytical work done on three dogs only will be given.

Dog 1.—This dog had eight analyses before any operation, in which the average gastric total acidity was 60. At his first operation the gall-bladder was filled with pebbles. This was followed by sixteen analyses, giving an average total acidity of 54. At a second operation on the dog the appendix also was filled with pebbles, which were held in place by purse-string sutures. The gall-bladder was examined at the time and found to be contracted and adherent to the liver. The stomach was free. The second operation was followed by nineteen gastric analyses, with an average total acidity of 75. At a third operation the appendix was found to be somewhat adherent to the bowels, but not entirely obliterated. More foreign bodies were placed in the appendix and this operation was followed by twenty-six analyses, with an average total acidity of 72. When, later, the animal was bled to death, many adhesions were found around the appendix, gall-bladder and intestines though the stomach was free from adhesions. The acidity had risen 25 per cent.

Dog 2.—This dog had seven gastric analyses, with an average total acidity of 43. The gall-bladder operation was followed by eight analyses, with an average total acidity of 42. This, again, was followed by an operation on the appendix and examination of the gall-bladder. This last operation was followed by eighteen analyses, with an average total acidity of 57, the last series of examinations showing an increased total acidity of 30 per cent. This dog, however, died from intestinal obstruction, and the last six analyses showed a gradual lowering acidity. At post-mortem examination it was found that dense adhesions about the appendix and bowels caused intestinal obstruction and death. It will be noticed, therefore, that, in spite of the gradual lowering of acidity in the last

six analyses prior to death, the last series of examinations, including the last six, had an increased acidity.

Dog 3.—This dog had thirteen gastric analyses, with a total acidity of 92. This was followed by an operation on the gall-bladder, filling the gall-bladder with pebbles. Eighteen analyses were then made, showing an average acidity of 82, a reduction of ten points. At a second operation the appendix was filled with pebbles and the stomach was found adherent to the gall-bladder and abdominal wall. Thirteen analyses were then made, with an average total acidity of 56. When the dog was finally bled to death, dense adhesions were found binding together the stomach, gall-bladder, intestines, appendix and omentum, and even the abdominal wall. This dog, therefore, showed a diminution of total acidity from 92 to 46, almost 40 per cent. The extensive adhesions certainly interfered with the gastric function.

From the analyses made on dogs subjected to operations, we were able then to draw two other conclusions. First, it was noticeable that dogs showing depression or shock following operation had a very uniform lowering of the gastric acidity. The acidity was also lowered when there were adhesions around the stomach, whether binding it to gall-bladder alone, or to the gall-bladder and bowels and abdominal wall. Second, it was noticed that those dogs which survived all operations, and which were examined post-mortem and found to have adhesions around the gall-bladder and appendix, which, however, did not interfere with the stomach and the gastric motility, had a very constant gastric hyperacidity. It will be noticed at once that the experimental work, though not as extensive as we should like, shows two features very similar to the clinical observations, namely, a decrease of gastric acidity following inflammation, shock or impaired gastric motility, and an increase of gastric acidity when the function of the perigastric organs only was impaired by adhesions and the stomach left free.

Bashford, at the head of the Imperial Cancer Research Laboratory, in London, reports the findings of the gastric analyses of 500 mice inoculated with cancer.

Most of the mice inoculated, of course, had cancer in organs not affecting the stomach. The analyses of these 500 mice showed a gastric hyperacidity. The hyperacidity could be explained only as a compensatory feature. This gastric hyperacidity of mice afflicted with cancer not affecting the stomach is quite a contrast to the hypo-acidity found in human beings afflicted with cancer affecting the stomach.

It will be noticed that this study of gastric secretions was not made on animals with the Pawlow fistula, inasmuch as the establishment of the Pawlow fistula, though ideal for certain studies of gastric secretion, would have required some adhesions between the stomach and the abdominal wall, which alone would have made rather indefinite a study of the influence of adhesions affecting the other organs, which concerned us more especially.

The terms "perigastric lesions" and "perigastric organs" have been used merely to avoid the more technical and frequent reference to the many abdominal structures and pathologic conditions either very close to or more distant from the stomach. There is no doubt that the functions of the liver, spleen pancreas and uterus, when changed by disease, have an influence on the stomach also.

CONCLUSIONS

It seems to me that this clinical and experimental study warrants the conclusion that the frequent diagnosis of nervous dyspepsia with hyperacidity should not be dismissed as a neurosis without caution. Likewise, many cases of hypo-acidity, even when occult blood and lactic acid are present in the gastric secretion, often demand an explanation beyond the stomach itself.

A summary of the experimental work showed, (1) a decrease of acidity during starvation; (2) an increase of acidity following excitement; (3) a decrease of acidity from lesions causing inflammation and shock

and greatly impaired motility; and (4) an increase, perhaps compensatory, when the function of the perigastric organ is impaired by adhesions. While this study, of course, is not conclusive it is reported simply as a matter of interest, with the hope that others interested in the physiology and diseases of the gastro-intestinal tract may investigate the subject more completely.

I wish to express my thanks to Drs. Stoner and Rogoff, who have done the many analyses with great care and labor and accuracy, as well as to Dr. Hambleton who did all the surgical operations on the dogs.

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ABSTRACT OF DISCUSSION

DR. DELANCEY ROCHESTER, Buffalo, N. Y.: In a paper presented by me before the Medical Society of the State of New York recently, fifteen or twenty observations were reported in which superacidity was noted in almost all, and it was stated that two factors brought this about. One was eyestrain, and the second was disturbance of the intestinal tract, or digestive tract below the stomach. Any disturbance in the digestive tract, such as duodenal ulcer, disturbance in the gall-bladder, gall-stones, adhesions around the duodenum, or around the pylorus, appendicitis, cholelithiasis, inflammation of the colon, chronic colitis, etc., all tend to produce superacidity of the gastric juice; in some cases gastric ulcer will develop which gives symptoms referable to points below, and the patient will not be cured of the symptoms until an operation has been performed; then the symptoms referable below the stomach will be relieved.

DR. JAMES T. PILCHER, Brooklyn: After a study of about 7,000 gastric analyses I wish to confirm Dr. Lichty's observations as regards the tendency to increased acidity of the gastric juice in cases in which there is gall-bladder involvement. However, as he so well pointed out, the other extreme is frequently encountered. While acknowledging the tendency to an increase of the hydrochloric acid content of the gastric juice in the majority of the cases of gall-bladder involvement in any of its many phases, I wish also to call attention to the fact that the other extreme may also be reached; in proof of this fact I will mention thirty-two cases of gall-bladder involvement and fifteen cases of combined gall-bladder and pancreatic involvement in which there was present, at the time of operation, a condition of achlorhydria hemorrhagica gastrica. Appreciating this, is is obvious that the conclusion that in all cases of gall-bladder involvement there is an increase in the

acidity of the stomach would be erroneous in the large majority of the instances, although it obtains, as has been noticed, in some 300 cases which I have had the opportunity of examining.

I wish further to congratulate Dr. Lichty on emphasizing so strongly and expounding so clearly the fact that in cases of so-called hyperchlorhydria we have not to do essentially with the stomach, but should seek the etiologic factor which is giving rise to reflex gastric symptoms. The question is certainly a pertinent one. Is there any such a condition as hyperchlorhydria *per se?* The indications certainly point against it and it will only be through such experiments as have been carried on by Dr. Lichty that we can come to any definite conclusions. The work so far accomplished I am sure is more than indicative that many of the dictums laid down so precisely in the text-books on the subject are in some respects fallacious and will shortly require a complete revision.

Dr. A. L. Benedict, Buffalo, N. Y.: The stomach is, to a large degree, an indicator of disease of other organs. For instance, in 100 serial "stomach cases" I found that 80 patients were either entirely normal so far as gastric secretion, etc., were concerned or, at most, showed only trivial gastric disturbances. The underlying condition was chronic colitis, typhlitis or even localized inflammation of the appendix, gall-stones, etc. Thus, we may well expect reflex variation in the condition of the stomach contents. Still, in actual practice, following a uniform technic, it is surprising to note that the analyses repeated in any given case, almost always give consistent results. Several years ago, in the American Gastro-Enterological Association, several cases of hyperchlorhydria due to gall-stones were reported. My experience is that gall-stones frequently give a typical clinical picture of hyperchlorhydria, more typical in fact than most cases of genuine hyperchlorhydria, but that on actual analysis, the stomach contents are of very low acidity. Do not understand me, however, as denying that there may be genuine hyperchlorhydria in gall-stone cases.

One more point: Many men speak of hyperchlorhydria as a common condition and one that can be diagnosed symptomatically. I do not believe that it can ever be positively diagnosed except by analysis. Furthermore, there is an unfortunate tendency both to exaggerate the degree of hydrochloric acidity and to accept a low standard of normal acidity. The hydrochloric acid of gastric juice is normally about 20 to 10,000, corresponding approximately to 50 degrees by N/10 alkali. For chyme, we may assume, approximately, a 50 per cent. dilution of gastric juice, making the normal standard of hydrochloric acidity one hour after an ordinary light test meal, about 25 degrees. To warrant the diagnosis of hyperchlorhydria, there should be either a considerable excess of

acidity by degrees or an excess of contents. My standard test meal consists of 50 grams of bread (one or two ordinary slices) 5 grams of butter (about what would ordinarily be spread on this amount of bread) and 250 c.c. of water (one glassful). By careful extraction, one should normally obtain from 30 to 100 c.c. one hour after such a meal. For such qualities, I should require a hydrochloric acidity of at least 40 degrees to establish the diagnosis of hyperchlorhydria, whereas, if there were an increase of chyme above the 250 c.c. ingested, any significant increase of acidity beyond the 25 degree standard, might be considered a basis for the diagnosis of hyperchlorhydria.

Now as to the exaggeration of the reading: using dimethylamido-azobenzol as an indicator, the end-point for free hydrochloric acid is at the transition from a distinct cherry red to a color almost exactly like that called cerise. We would naturally suppose that cherry-red and cerise meant the same tint but they do not. Beyond this end-point, the further addition of alkali produces changes, through orange to a straw yellow, for somewhere about 10 or even 15 degrees. One can readily see that a man who titrates to the final change, in estimating his free hydrochloric acid and perhaps overruns, at that, and who has started with the assumption that anything beyond 20, or perhaps 15 degrees of free hydrochloric acidity, is an excess, will find hyperchlorhydria, not only in normal cases, but in those in which there is a moderate hypochlorhydria—hence, a lot of nonsense about hyperchlorhydria associated with organic fermentation.

Dr. G. C. Smith, Boston: Ewald, several years ago when lecturing to students who came to him from all over the world to study diseases of the stomach, made the statement that 98 per cent. of all diseases with symptoms referable to the stomach originate from outside the stomach.

Dr. Gustav Baar, Portland, Ore.: What do we want to know when we see these cases? Shall we, as internists, attempt to cure these patients, or shall we turn them over to the surgeon? What are the additional signs and symptoms we can have besides hyperacidity which will enable us to determine whether we are dealing with some gastric trouble or with some extragastric trouble—appendicitis, perigastritis, etc.? In an examination of 10,000 urines, routine tests were made for indican and in nearly all hyperacidity cases caused by extragastric disturbances it was found constantly present. The constant presence of excessive indican in the urine means some anatomic disturbance of the gastrointestinal wall and calls for surgery.

Dr. John A. Lichty, Pittsburg, Pa.: I have noticed in my clinical experience that many patients have consulted me for disturbances of the stomach when, in truth, the trouble was elsewhere. Many of them had hyperacidity and often there

was a high percentage of free hydrochloric acid. They had also the typical symptoms of hyperchlorhydria. Many had been treated previously from time to time as "nervous dyspeptics." Three or four years ago, when at Leeds, I had an opportunity of referring to these cases in conversation with Mr. Moynihan who impressed on me the fact that these patients were probably suffering from duodenal ulcer and might at any time have perforation. When I returned to my work, I continued my observations, but did not see a single instance of perforating duodenal ulcer. I did, however, find every now and then one of these patients with an attack of acute appendicitis or an attack of gall-bladder or gall-duct trouble, and, at the operation, the pathology revealed, always showed that attacks must have occurred previously, the history of which I was unable to get, and that the whole train of symptoms must have been due to the lesion found. It occurred to me that probably hyperchlorhydria was an accompanying symptom of gall-bladder, or appendix affection. For this reason, I experimented on dogs to determine whether a foreign body in the gall-bladder or in the appendix or the adhesion produced might not produce the same disturbance of gastric function as is found clinically. The Ewald test breakfast was used and every effort was made to make the experiment conform with the technic used clinically. Six dogs were under observation. One was kept for a control dog. Of the five dogs in which the gall-bladder was opened, and an infected foreign body introduced, all but one subsequently showed an increased acidity and a diminished gastric motility. These results are in accord with the paper which has just been read.

Dr. M. J. Lichty, Cleveland, Ohio: It has been noticed for some time that frequently gastric disturbances are present clinically, when the real trouble has been in other organs; just why this is so does not seem entirely clear to us at present. We frequently see high acidity of the gastric juice when there are gall-stones; and the high acidity disappears on the removal of these gall-stones. I have in mind an individual who had gall-stones and with this condition a high acidity, but when the gall-stones were removed the man became perfectly well. I am glad that Dr. Pilcher has called attention to the terms hyperacidity and hypersecretion. I did not mean to use them synonymously in the paper. Of course the terms signify different conditions, and these two conditions should be studied more both clinically and experimentally.

The question has been asked, What shall we do with these cases of disturbed secretions? We certainly should not subject all these patients to operation at once, though when these rather obscure cases do not improve under systematic treatment, they should require further study and operation may be necessitated. A patient recently referred to me on account of stomach trouble had no symptoms whatever except vomit-

ing which had existed for weeks. At my first examination, I found some tenderness over McBurney's point and was rather confident that there was an unrecognized appendicitis. Operation proved it so and removed the symptoms.

I recall another patient who had gastric symptoms, but in whom I noticed, after repeated examinations, an occasional slight tenderness over the region of the appendix. This patient has been treated some years before for gastro-intestinal trouble by a physician whose practice is now confined to surgery. The same man was called in consultation and hesitated to confirm the diagnosis of chronic appendicitis. At last he approved of operation; and when he operated he could hardly find the little appendix, half obliterated and buried with many dense adhesions; but while removing it with great difficulty he remarked: "Here was likely the trouble when I treated this patient eleven years ago for dyspepsia."

CLINICAL RESULTS OF GASTRO-ENTEROSTOMY FOR NON-MALIGNANT DISEASES

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There have been very few accurate and thorough reports on the results of gastro-enterostomy for ulcer of the stomach.

Bettman and White[1] have collected reports of 150 cases with results after the lapse of at least one year. Bamberger[2] has studied 836 cases in which operation was performed for chronic ulcer of the stomach. The former study shows an immediate mortality of 10 per cent., the latter, 12.2 per cent. To this must be added a late mortality from complications in Bettman and White's series of 14.6 per cent. and in Bamberger's cases of 5 per cent. (complete late reports lacking in many of Bamberger's series).

We find, then a total mortality of 24.6 per cent. in one series and 17.2 per cent. in the second series. The group of 836 cases showed 74 per cent. cures; 13.4 per cent. unchanged. In the group of 150 cases there were 60 per cent. of cures and 30 per cent. of deaths, or no improvement.

The basis of the present report consists of forty-eight cases in which the patients were personally examined before operation; in all but two cases tests of the stomach

1. Bettman and White: Med. Rec., Oct. 9, 1909.
2. Bamberger, L.: Die innere und die chirurgische Behandlung des chronischen Magengeschwurs und ihre Erfolge, Julius Springer, Berlin, 1909.

TABLE 1.—IMMEDIATE MORTALITY (WITHIN SEVENTEEN DAYS)*

Case.	Year.	Sex.	Age.	Diagnosis.	Gastric Findings. HCl.	Total Acidity.	Cause of Death.	Time After Operation.	Operation.
1.	1903	M.	60	Pyloric ulcer; arteriosclerosis; previous medical treatment.	80	110	Shock.	24 hours.	Gastro-enterostomy.
2.	1903	M.	56	Multiple ulcer of pylorus and duodenum; slight stenosis.	84	112	Shock.	48 hours.	Gastro-enterostomy.
3.	1904	M.	74	Ulcer of lesser curvature near pylorus; no stenosis.	65	85	Shock.	6 hours.	Gastro-enterostomy.
4.	1904	M.	51	Pyloric ulcer; stenosis; previous medical treatment.	60	80	Hematemesis.	6 days.	Gastro-enterostomy.
5.	1904	M.	63	Pyloric ulcer; stenosis.	10	20 Retention.	Vicious circle.	12 days; 6 hours after second operation.	Gastro-enterostomy.
6.	1905	M.	30	Pyloric ulcer; no stenosis.	60	84	Vicious circle.	10 days.	Gastro-enterostomy.
7.	1906	F.	30	Hour-glass stomach near pylorus.	0 Lactic.	2 Retention.	Shock.	12 hours.	Resection pylorus; Gastro-enterostomy.
8.	1906	M.	45	Perforating pyloric ulcer; stenosis.	43	68 Retention.	Gangrenous appendicitis.	17 days.	Resection pylorus; Gastro-enterostomy.
9.	1906	M.	36	Duodenal ulcer; slight stenosis.	20	34 Retention.	Perforation and peritonitis	3 days.	Gastro-enterostomy.
10.	1908	M.	65	Pyloric ulcer; old perforation; localized abscess; stenosis.	No tests.		Peritonitis.	10 days.	Gastro-enterostomy.
11.	1909	F.	35	Hematemesis; clinical diagnosis ulcer; no visible ulcer or stenosis.	No tests.		Shock.	24 hours.	Gastro-enterostomy.
12.	1910	M.	61	Pyloric ulcer (active); stenosis.	60	90	Hematemesis.	48 hours.	Gastro-enterostomy.

* Average age, 50.5 years; immediate mortality, 25 per cent.; males 10; females 2.

TABLE 2.—LATE MORTALITY *

Case.	Year.	Sex.	Age.	Diagnosis.	Gastric Findings. HCl.	Total Acidity.	Cause of Death.	Time After Operation.	Operation.
13	1901	M.	30	Active pyloric ulcer; stenosis.	0	6 Retention.	Recurrent hematemesis.	3 months.	Gastro-enterostomy.
14	1908	M.	63	Duodenal ulcer; localized ulcer;	70	85 Retention.	Carcinoma ventriculi.	6 mos. after first operation.	Gastro-enterostomy.
15	1908	F.	34	Pyloric ulcer; stenosis.	23	46 Retention.	Carcinoma ventriculi.	21 mos. after first operation.	Gastro-enterostomy.

* Total mortality 31.25 per cent.; males 12; females 3; mortality since 1906, 10.41 per cent.; seven hyperchlorhydria; four hydrochloric acid normal; two hydrochloric acid absent; two not determined.

contents and motility were performed. In fifteen cases examinations of stomach functions were made previous and subsequent to the operation. Forty-six patients were operated on by local surgeons, one by Dr. W. J. Mayo and one in Lausanne, Switzerland.

Fifteen patients have died, twelve within 17 days of the operation; an immediate mortality of 25 per cent.; a total mortality of 31.25 per cent; mortality since 1906, 10.41 per cent. The predominance of males (twelve males, three females), is significant. The average age is 50.5 years.

Case 8 was instructive. The patient was a man, aged 45, alcoholic, with a history of ulcer for five years with frequent severe hematemesis. Operation had been repeatedly refused. An ulcer on the anterior aspect of the stomach adjoining the pylorus was found which ruptured during manipulation. Partial gastrectomy with gastro-enterostomy was done. The patient made an uneventful recovery for fifteen days; then peritonitis developed to which he succumbed in two days. Necropsy revealed a ruptured gangrenous appendix with localized peritonitis. The site of operation was not involved. This case is an argument in favor of appendectomy with every gastro-enterostomy.

The three later deaths were due to carcinoma ventriculi in two instances, one six months, one twenty-one months after operation. In each case the patient had apparently recovered. Possibly these two ulcers had already undergone carcinomatous transformation at the time of operation. The third death resulted from recurrent hematemesis, morphinism and asthenia.

Of the fifteen fatal cases hyperchlorhydria was present in seven, anacidity in two, normal acidity in four, no determination in two. Evidence of retention of chyme was found in seven cases. Five of the patients who died had been treated medically without success. Eight patients received desultory treatment, no correct diagnosis having been made. Surgical treatment should have

been given much earlier in these eight fatal cases, as shown by the advanced degree of stenosis seen at operation. Two patients (3 and 11) should not have been operated on as no stenosis was found. Recent histories have been obtained in twenty-nine of the thirty-three patients living.

Table 3 gives the data in fifteen cases in which gastric analyses were made before and at varying periods after operation. The average age at time of operation was 43.2 years. There were nine males and six females. In this group twelve had ulcer of pylorus or duodenum with stenosis; one, ulcer of pylorus without stenosis, (Case 18); another had nervous dyspepsia (Case 20) and one atony of the stomach with dilatation.

Seven patients with ulcer and stenosis made perfect recoveries, while three recovered but are obliged to abstain from acid and indigestible foods.

Another case (18) has improved, but has recurrent hematemesis and morphinism.

In Case 20 gastroplication was performed, leaving the patient with an aggravation of symptoms.

In Case 28 (nervous dyspepsia) the gastro-enterostomy has been followed by greater suffering than before the operation.

Examination after an Ewald test breakfast shows free hydrochloric acidity above 40 in six cases, between 20 and 40, or normal in two; below 20 in six; absent in one.

Hyperchlorhydria has increased after operation in three cases (Nos. 16, 19, 25). One of these patients (No. 16) has regained motor power and is free from symptoms when he refrains from acid and heavy foods. The second (No. 19) has retention of chyme for ten hours, a greater hyperchlorhydria with a complete recovery from all gastric disturbances.

Hyperchlorhydria has disappeared in three cases (Nos. 21, 29, 30) and the proper motor function has been restored.

47.	1907	F.	30	Pyloric ulcer; cholelithiasis; stenosis.	Gastro-enterostomy.	Operative	Recovery.	60	Retention. 80		1
48.	1909	F.	25	Pyloric ulcer; no stenosis.	Gastro-enterostomy.	Operative	Recovery.	40	No retention. 60		2

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TABLE 4.—RESULTS IN 12 CASES, 1 TO 6 YEARS AFTER OPERATION

Case.	Year.	Sex.	Age.	Diagnosis.	Operation.	Result.	Gastric Findings HCl.	Gastric Findings Total Acidity.	Last Report After Operation. Years.
31.	1903	M.	28	Pyloric Ulcer; perigastric adhesions.	Gastro-ent.	Perfect.	22	44	5
32.	1903	M.	45	Pyloric ulcer; stenosis.	Gastro-ent.	Improved.	30	75	1
33.	1904	F.	31	Pyloric ulcer; stenosis.	Gastro-ent.	Improved; has hyperchlorhydria.	40	60	2
34.	1904	M.	45	No ulcer or stenosis; nervous dyspepsia.	Gastro-ent.	No improvement; worse.	54	78	2
35.	1904	F.	50	Pyloric ulcer; stenosis.		Recovery.	65	85	6
36.	1905	F.	30	Pyloric ulcer; perigastric adhesions; no stenosis.	Gastro-ent.	Made worse; vomiting.	30	50	5
37.	1905	F.	57	Pyloric ulcer; stenosis.	Gastro-ent.	Perfect.	4	10	5
38.	1907	M.	48	Duodenal ulcer; partial stenosis.	Gastro-ent.	Perfect.	69	84	3
39.	1908	F.	24	Pyloric ulcer; stenosis.	Gastro-ent.	Perfect.	50	80	2
40.	1908	M.	60	Pyloric ulcer; stenosis.	Gastro-ent.	Perfect.	19	43	2
41.	1908	F.	37	Pyloric ulcer; stenosis.	Gastro-ent.	Perfect.	50	80	2
42.	1909	M.	59	Duodenal ulcer; stenosis.	Gastro-ent.	Perfect.	36	92	1

TABLE 5.—SIX CASES IN WHICH LATE RESULTS COULD NOT BE SECURED

Case.	Year.	Sex.	Age.	Diagnosis.	Operation.	Result.	Gastric Findings HCl.	Gastric Findings Total Acidity.	Last History After Operation. Months.
43.	1905	F.	35	Ulcer lesser curvature; pyloric stenosis.	Gastro-enterostomy.	Operative Recovery.	60	80	2
44.	1906	M.	40	Pyloric ulcer; stenosis.	Gastro-enterostomy.	Operative Recovery.	28	50	1
45.	1907	F.	22	Pyloric ulcer; no stenosis.	Gastro-enterostomy.	No relief.	25	35	3
46.	1907	M.	42	Duodenal ulcer; slight stenosis.	Gastro-enterostomy.	Improved.	25	40	2
47.	1907	F.	30	Pyloric ulcer; cholelithiasis; stenosis.	Gastro-enterostomy.	Operative Recovery.	60	80	1
48.	1909	F.	25	Pyloric ulcer; no stenosis.	Gastro-enterostomy.	Operative Recovery.	40	60	2

Patient 20, in spite of a clinical history of ulcer with hematemesis, had no visible ulcer scar or stenosis. Five years after operation hydrochloric acidity is within normal limits and motor power is perfect.

Patient 23, who had normal acidity, has two years after operation persistence of motor insufficiency and no improvement in condition. The six patients with hypo-acidity have suffered a variety of results. Patient 17 has developed a hyperchlorhydria, has a good motor function and is free from symptoms if he abstains from acid foods.

In Cases 18, 24 and 27 the hypo-acidity has been supplanted by an absence of free hydrochloric acid. In Case 23 the hydrochloric acid has risen to a normal degree and motor power has become established, while in Case 28 the hydrochloric acid has decreased and retention of chyme continues with the patient unimproved. Before operation Patient 26 had an absence of hydrochloric acid with marked retention of chyme. The hydrochloric acid has not reappeared, drainage is now complete within the normal time.

The appearance of bile has usually been noted one hour after the test breakfast, for four months, after which it cannot be detected. Bile was found, however, in Case 18 four years after operation.

Table 4 outlines twelve cases in which results have been ascertained from one to six years after operation. Six cases are included in which operative recoveries only are procurable (Cases 31 to 48, inclusive). In this group the diagnosis is chronic ulcer of the stomach with stenosis in fourteen; chronic ulcer without stenosis in three; nervous dyspepsia in one.

The following outline shows results in the entire series of 27 patients known to be alive.

ULCER OF STOMACH OR DUODENUM WITH STENOSIS.	21
Perfect recovery	14
Recovery (care required as to choice of food)	4
Improved	2
Unimproved	1
	21

ULCER OF STOMACH OR DUODENUM WITHOUT STENOSIS, 3	
Perfect recovery	1
Improved	1
Unimproved	1
	3
NERVOUS DYSPEPSIA, 2	
Unimproved	2
ATONY WITH DILATATION, 1	
Unimproved	1
Total	27

A definition of the term "perfect recovery" as used in this classification depends on unqualifiedly favorable answers to the following questions:

Do you still have trouble with your stomach? Do you have any belching of gas or food? Do you vomit at all? Have you vomited or spit up any blood since the operation? How is your appetite? Do you find it necessary to eat more than three meals a day? Are your bowels regular or do you find it necessary to take physic for them?

There must also have been the ability to pursue the former vocation or avocation without disturbance.

The elimination of three cases of nervous dyspepsia, one of gastric atony and one in which no determination was made enables us to discuss the gastric findings in forty-three undoubted cases of ulcer of the pylorus or duodenum.

	Cases.
Hyperchlorhydria (free hydrochloric acid above 40)	19
Normal acidity (free hydrochloric acid 20-40)	14
Hypoacidity (free hydrochloric acid below 20)	7
Anacidity (free hydrochloric acid absent)	3
Total	43

This makes nineteen patients with hyperchlorhydria; twenty-four patients with normal or subnormal hydrochloric acid.

CONCLUSIONS

1. Hyperchlorhydria as a symptom of chronic gastric ulcer is inconstant and should be disregarded.

2. Perfect recovery may occur when atony of the stomach has existed before the development of ulcer and motor insufficiency persists; illustrated in Case 19.

3. Many of the fatalities cited in this report would have been averted had the family physician made a diagnosis before serious complications had developed. Forty patients in this series of cases gave a history of ulcer covering five years or more before the diagnosis was made.

4. Pylorectomy offered a better prognosis for recovery in five of the fatal cases. Patients 4, 12 and 13 were lost by fatal hemorrhages from the ulcer area. Patients 14 and 15 died as a result of carcinomatous transformation of the pyloric ulcer.

5. The legitimate field for gastro-enterostomy in benign diseases of the stomach is in chronic ulcer near or below the pylorus with stenosis.

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ABSTRACT OF DISCUSSION

DR. JUDSON DALAND, Philadelphia: Chronic gastric ulcer often shows a period of latency so far as the symptoms are concerned, although the ulcer itself is still present. The patient seems to recover symptomatically. It is believed that no ulcer is present at all and the case is often pronounced cured. I recall one case in which the funicular ulcer was discovered and removed; this was followed by complete recovery. The cases of gastric ulcer referred to at another session of the Section in which the carcinoma was supposed to be cured three times belong to this same group. We see cases of chronic indolent ulcer in which under treatment great improvement results and the patients are supposed to be well.

DR. MILTON J. LICHTY, Cleveland, Ohio: The study of these cases and the study of the statistics ought to be of great value and help to physicians. I should like to remind the members of the Section of the discussion of this subject three years ago by Dr. Paterson of London, when he spoke of the value of gastroenterostomy in connection with cases of gastric ulcer. He reminded us of the temporary benefit to be derived from gastroenterostomy when there was incomplete stenosis of the pylorus. I have watched cases since and must say that the best results of the gastroenterostomy were seen in cases in which the stenosis was almost absolutely complete. One does not really know just what to do with cases of incomplete stenosis of the pylorus. Of course, we cannot dictate to the surgeon just what shall be done at the time of operation, but it seems to me that in some cases in which a gastroenterostomy has been done, the patient's subsequent condition shows

that it would have been better to have done a pylorectomy. It seems also that a pylorectomy should be the operation of choice whenever possible, and that a gastroenterostomy should only be done when there is complete stenosis of the pylorus.

DR. JOHN A. WITHERSPOON, Nashville, Tenn.: A few years ago a very prominent surgeon regarded this disease as a surgical one. The pendulum has swung back now, and every advanced surgeon is doubting the propriety of operating on gastric ulcer unless there are definite evidences of obstruction. I do not feel that gastric ulcer belongs to the surgeon for two reasons. Operation in my experience in the past has been unsuccessful. The patients I have had have recovered immediately, but later they had more or less trouble. Some of the bad ulcers become latent. It is extremely difficult in some cases to determine whether or not the gastric ulcer is cured; we know that often by medical treatment alone we may relieve patients symptomatically and they may get along well for months, gaining flesh. Yet the condition may remain dormant for some time only to awaken into activity again. A few years ago every case of hemorrhage from the stomach in cases of ulcer was referred to the surgeon for treatment; recently it has been found that medical treatment is better in such cases. The surgeon will not intervene now unless there is complete obstruction; then surgery may save many lives which otherwise would be sacrificed.

DR. DELANCEY ROCHESTER, Buffalo, N. Y.: If there is impending obstruction, or actual obstruction, of course immediate operation is indicated. However, a gastroenterostomy is an operation that I believe should be avoided wherever possible. If any operation is to be done at all I should say that the one to be preferred was pylorectomy. I agree with Dr. Witherspoon that much can be done by medical and dietetic treatment in these cases and an operation should not be urged on patients with gastric ulcer unless it is absolutely necessary, because of the danger of cancer developing. This is a possibility, although a possibility only. Such good results are obtained from medical and dietetic treatment if continued for a sufficient length of time that operative measures should be avoided if possible.

DR. A. J. BENEDICT, Buffalo, N. Y.: My experience with gastroenterostomy for either malignant or non-malignant disease of the pylorus is limited to one or two cases, because such an operation seemed inadvisable. In cases in which there is marked obstruction at the pylorus, a superior enterostomy is a good substitute for gastoenterostomy, the idea being to short circuit the stomach. In patients with serious lesions of the stomach the chances for betterment are increased if no food passes through this organ at all. In one patient, a woman on whom superior enterostomy was performed, a diagnosis of carcinoma was made. The patient was very much

emaciated; there was pyloric obstruction and there was no free hydrochloric acid. I thought that I could feel the thickened pylorus and when the tube was passed, obstruction was also found at the cardiac end. The surgeon who was called in wanted to do gastroenterostomy, but it was decided that a superior enterostomy was to be preferred. On exposing the stomach there was found a small tumor at the pylorus. A section was not made, but taking it for granted that the tumor was a cancer, enterostomy was performed, and the patient was nourished through the fistula in the small intestines. I wish to emphasize that the diet should be watched with care. In the course of three or four weeks the symptoms in this patient were somewhat relieved; however, she had so much mental distress because of the fistula that we decided to close it, believing that she would die soon anyhow. That was in 1898. To our surprise, the woman made a good recovery and has remained well ever since. The tumor could not have been a cancer; just what it was I do not know.

DR. GUSTAV BAAR, Portland. Ore.: It seems to me that a mortality of 20 per cent. is too high in such cases. I have had sixteen patients operated on by surgeons during the last few years, and none died. Two of these cases were most remarkable. One patient was a woman of sixty, six feet tall, with a palpable tumor and with frequent hemorrhages; she was much emaciated, weighing but ninety-eight pounds. A gastroenterostomy was performed, and the surgeon thought that he was dealing with a carcinoma. I insisted, however, on the diagnosis of an indurated ulcer. There was free hydrochloric acid present. The patient took nourishment without the slightest distress, being given lamb chops on the third day after operation. At the end of two months her weight had increased to 168 pounds. This was only two years ago; the patient, at this date, is perfectly well. In another case the tumor was the size of the fist and appeared in a man aged forty-five. He had repeated hemorrhages. A diagnosis of indurated ulcer was made and a gastroenterostomy was performed. The man was absolutely cured. I believe that gastroenterostomy gives the most satisfactory results in all cases of pyloric ulcer and is a real boon to suffering humanity.

DR. JOHN D. DUNHAM, Columbus, Ohio: In regard to the symptomatic cure of these patients I wish to emphasize the fact that such patients should be followed for a number of years before any final conclusions regarding them should be considered. The surgeon who sees these cases finds the patients sufficiently recovered to leave the hospital and he cites such cases as recoveries. However, the general practitioner who follows the cases will often find recurrences. In the series of cases reported there was only one in which a secondary operation was called for. If the cases are properly selected

and only those patients with stenosis are operated on, a secondary operation will rarely be needed. Attention to the diet is very important. These patients with partial or complete pyloric stenosis are starved, as a rule, and they require abundant feeding; they cannot live on slops; the choicest and best food properly prepared should be given them for many weeks. The food should be given frequently through the day and not as is customary, three times a day. In a consideration of the mortality the surgeon includes only the deaths which occur immediately after the operation, while the general practitioner and the internist follow the patient's history for several years. The mortality after gastroenterostomy should only be considered when the cases have been studied for five or six years. In the series I reported there were two cases in which perforation of the stomach occurred and two in which carcinoma developed.

PRELIMINARY REPORT ON THE CLINICAL SIGNIFICANCE OF INDICANURIA

BASED ON TEN THOUSAND EXAMINATIONS FOR INDICAN

G. BAAR, M.D.
PORTLAND, ORE.

In the last four years I have made it a routine practice to examine the urine of every patient for indican. Jaffe's test, carried out as follows, has been employed:

The urine was precipitated with lead acetate (moderate quantity), filtered through a dry filter-paper, and an equal quantity of fuming hydrochloric acid with ferric chlorid (50 c.c. hydrochloric acid, with 8 to 10 drops ferric chlorid) added to the precipitate. This was shaken thoroughly for two minutes, then shaken with 1 c.c. chloroform for the same length of time.

The depth of the blue discoloration of the chloroform was taken as indicating the quantity of indican present; thus designating the quantatives as "very excessive," "excessive," "considerable," or "moderate." Traces of discoloration were not taken into consideration. In 10,000 urine examinations I found indicanuria present in about one-third of the cases, mostly, however, temporarily only and I designated these as "accidental indicanurias." The cases, however, in which there appeared constantly excessive indican, which formed the most conspicuous clinical symptom of the case, I called "indicanuria par excellence." Cases in which the examination of the whole body, the stomach contents, the feces and blood did not yield any abnormal findings, but in which indican in the urine appeared constantly in excessive quantity I considered "intestinal auto-intoxica-

tion," provided the complaints of the patient pointed, even though uncertainly, to the digestive apparatus. I wish to state here in advance that true cases of intestinal auto-intoxication are rare. This statement, I am well aware, places me in direct opposition to the general profession as held to-day. Such patients present clinically the following symptoms: pale complexion, dry skin, cold hands, and feet, dizziness, headaches, insomnia, nervous depression, neuralgias, migraine, rheumatic pains in the extremities, emaciation, fetor ex ore, often acne, seborrhea, furunculosis, and urticaria. The excessive amount of indican in the urine of these patients indicates simply the large increase in the sulpho-ethers and aromatic substances of the urine.

The indoxyl compounds are not toxic in themselves. So far as we know they are not capable of producing any such pathologic symptoms as enumerated above. The true toxic substances are the ptomains. The "aromatic bodies" (phenols, cresols, indol, skatol), however, develop in parallel degree with the former in intestinal putrefaction. While we do not possess a simple clinical procedure to estimate the ptomains, we do possess one in the above-mentioned Jaffe's test, which permits a practical estimation of the aromatic bodies and thus gives valuable information as to the metabolism of the body; for it is a proved fact that whenever ptomains are absorbed from the intestinal tract sulpho-ethers of the aromatic bodies are absorbed simultaneously, and by measuring the quantity of the sulpho-ethers we obtain knowledge of the intensity of the putrefactive processes within the bowel. There are but two exceptions to this rule: (1), individuals taking aromatic drugs internally, i. e., salol, phenol, naphthol; (2), organic suppurations. In this manner the excessive excretion in the urine of sulpho-ethers and aromatic compounds serves as an indicator of an abnormal formation and absorption of the products of microbic nitrog-

enous putrefaction. The intestinal anaerobic flora being one of putrefaction, we find it always predominating in cases of intestinal putrefaction.

It is not, however, the quantity of putrid substances formed in the bowel, but the quantity of those putrid substances entering the blood which causes the symptoms of auto-intoxication. This accounts for the fact that, on the one hand, we may find in cases of marked intestinal putrefaction many toxins in the stool but few only in the blood. Diarrhea, for instance, or mucus covering the intestinal mucosa, diminishes their passage into the circulation; and so also will perfect function of the other organic lines of defense, to wit, liver, kidney, pancreas, prevent their absorption. On the other hand, however, even a feeble intestinal putrefaction will cause auto-intoxication if the lines of defense are broken, owing, for instance, to deep ulcerations of the mucosa or insufficient function of the antitoxic organs. Thus we may explain the case of a young girl, who suffered with a bloody purulent diarrhea for eight months, not showing any indican in the urine but frequently excessive amounts in the feces. When an appendicostomy was performed on this patient for the purpose of irrigating the colon, the urine, which never before showed indican, showed excessive amounts of indican on the four days following the operation, together with distinct traces of bile.

These findings prompted me to examine urines of patients to be operated on, before and after operation. The following are some of the conclusions I reached:

1. Ether narcosis has no influence whatever on the excretion of indican.

2. In all gastro-enterostomies, entero-anastomoses, appendectomies—in all operations, in short, in which the intestinal wall was cut, we found excessive indican and distinct traces of bile in the urine for a week or more following the injury.

3. Moderate handling of the intestines during the course of an abdominal operation did not cause any indican to appear in the urine, while prolonged handling of the intestines did cause excessive indican in the urine.

These findings offer the quasi-experimental evidence for my assertion that the trauma to the intestinal wall with the subsequent inflammatory and functional changes of the latter cause the impairment of the absorptive powers of the mucosa, thereby increasing intestinal putrefaction; an indicator for this increased putrefaction is the amount of indican excreted in the urine. The clinical evidence for my claim is given by the fact that the majority of my chronic appendicitis cases showed excessive amounts of indican in the urine, more especially during the recurrent attacks. The same did all mucous colitis cases. The mucous coating of the colon in these cases inhibits the toxicolytic functions of the mucous membrane, favoring, thus, intestinal putrefaction.

The thought that mechanical trauma to the intestinal wall is sufficient to produce indican was instrumental in my diagnosing four cases of pericholecystitis adhesiva, in which the diagnosis was corroborated by the surgeon. One case was that of a man aged 45, who had suffered almost constantly for twenty years with ill-defined painful sensations in the right and upper abdominal region. The examinations of the urine made frequently after such attacks showed always the presence of considerable indican and distinct traces of bile. On further inquiry the patient remembered an icterus he had had about twenty years before. The operator found the suspected adhesions between the right flexure of the colon and the gall-bladder. The severance of these adhesions brought a complete recovery of the patient, who had been considered all his life a neurasthenic only. The very same condition existed in another case, that of a middle-aged

woman whose gall-bladder was found completely adherent to the colon. The excision of the gall-bladder effected a cure. Similar pathologic conditions existed in the two remaining cases. In one of them there was also present an adhesive chronic appendicitis. For the explanation of the constant presence of distinct traces of bile during the painful attacks, I merely suggest the kinking of the bile-duct, brought about mechanically by the peristalsis of the colon adherent to the gall-bladder, thus causing a temporary entrance of bile into the circulation.

The same principle of prolonged mechanical trauma to the intestinal wall through coprostasis explains the asthenic condition present in more than 300 cases of enteroptosis I tested repeatedly for indican. While it must be admitted that gastroptosis and enteroptosis are primary conditions, as Glenard and Stiller have proved, it will be easily understood that the "transverse festoons" of the intestines predispose to coprostasis. As long as the latter takes place in the rectum alone—either by its atonic or its spasmodic condition—on account of the dryness of the feces and consequent diminution of the number of bacteria, it will not cause putrefaction. This is proved by the cases of constipation in adults as well as in children, with periods of three to ten days between bowel movements, without the appearance of any of the phenomena of putrefaction, including no indican in their urine. If the coprostasis, however, takes place in the cecum or ascending colon, where there is not yet dryness of feces, but humidity and often alkaline reaction, the most favorable conditions for exaggerated putrefaction are created. The toxins, ammonia compounds and sulphuretted hydrogen, which then enter the portal vein from the intestinal tract, destroy red blood-cells in the portal system. The hemoglobin thus liberated is carried into the liver where it is found deposited in the hepatic cells as blackish

granules, containing iron from the bloodpigment. Thus we could find in almost all cases of enteroptosis anemias of about 70 per cent. (Sahli) and 4,500,000 red blood corpuscles. By applying a well-fitting abdominal supporter to these patients, rendering better defecation possible and at the same time fattening them, most of these patients became free of indican and attained normal blood again.

Quite conspicuous was the constant finding of indican in those cases of constipation, which were complicated by cardiac insufficiency. This latter must needs produce an insufficiency of digestive juices which can explain the formation of enterotoxins from the undigested residua attacked by bacteria. The same explanation holds true in all the accidental indicanuria cases, including febrile diseases, cachexias, nervous diseases (tabes, cerebral tumors, meningitis).

Schmidt's "intestinal dyspepsia"—a functional disease of the small bowel, in which the carbohydrates are not utilized—is very rare. In many hundreds of stool examinations I have found only a few instances in which exaggerated fermentation was obtained in the first twenty-four hours in Schmidt's apparatus. In none of these cases was there any indican present in the urine.

Among the chief emunctories for those products of intestinal putrefaction which are circulating in the blood (like indoxyl, skatoxyl, phenol, leukomains, etc.) rank the kidneys. Any renal insufficiency therefore should—according to Combe's opinion—lead to a retention of the above mentioned products, i. e., "auto-intoxication." It is noteworthy that in a few thousand of indican tests made on patients with acute and chronic diffuse nephritis, pyelonephritis, tuberculosis of the kidneys, indican was found relatively rarely, and there were hardly any symptoms of the much-dreaded "auto-intoxication" present. Interesting in this respect was

the case of a young woman with pyuria, due to a tuberculous abscess in the left kidney. For many weeks prior to the excision of the left kidney her urine never showed any trace of indican; since the removal of her diseased kidney, however, the urine—though practically free of pus—shows constantly considerable amounts of indican, while the woman herself feels perfectly well in every respect.

The liver is credited with the exercise of a powerful toxicolytic function against the enterotoxins entering the same through the portal vein. Diseases of the liver cells, should favor intestinal putrefaction, thus increasing the aromatic bodies in the urine. About a hundred cases of liver diseases like hypertrophy, cirrhosis, syphilis of liver, cholangeitis, and carcinoma hepatis were studied in regard to their relation to indican excretion. I have come to the conclusion that indicanuria exists only in extreme hepatic insufficiency, when the latter is indicated not only by the decrease of urea in the urine—"hypo-azoturia"—but by the simultaneous presence of leucin and tyrosin in the same. While a marked increase in the sulpho-ethers and aromatic bodies always indicates auto-intoxication to a certainty, its hepatogenous origin should be asserted only by considering the amount of urea and leucin in the urine at the same time; for we know that urea is formed in the liver from the amino-acids and ammonia carried into it through the portal vein from the intestines; and uric acid is similarly formed in the liver from the nucleins and xanthic bases. Hepatic insufficiency, therefore, implies decrease in urea and uric acid. If urea was not decreased, we should have to think of some other origin for the auto-intoxication. If, however, in addition to a decrease of urea I found that 150 gm. of glucose produced alimentary glycosuria, my assumption of a general hepatic insufficiency would be strengthened. Thus I could see —though rarely—"auto-intoxication" brought about

through hepatic insufficiency in cases of normally functionating intestines.

Normal gastric juice is supposed, under normal conditions, to either destroy or at least diminish the number of bacteria which cause putrefaction. In more than five hundred examinations of the gastric contents I found that hyperacidity quite frequently was coupled with indicanuria. If there was simultaneously present ulcer of the stomach or duodenum, indicanuria was always present. Hyperacidity coupled with indicanuria indicates an extragastric lesion, like chronic cholecystitis or appendicitis, provided ulcer of stomach or duodenum can be excluded. More than twenty laparotomies corroborate thus the value of indicanuria for the differential diagnosis between gastric and extragastric lesions. Cases of anacidity and hypacidity showed indicanuria only in half their total number. Whenever these conditions were accompanied, however, by carcinoma ventriculi, indicanuria was always present.

The insufficiency of pancreatic juice (the tryptic action of which neutralizes many toxins) with its consecutive increase of intestinal putrefaction was shown in two cases of carcinoma of the pancreas with ever-present excesive indican.

Bile insufficiency is supposed to cause intestinal putrefaction, partially owing to the absence of the antitoxic action of taurocholic acid, partially because it leaves a larger alimentary residua for the bacteria to prey on. About fifty cases of icterus, with complete occlusion of the common duct, caused either by gall-stones or catarrhal icterus, showed indicanuria in but ten cases. Among these fifty cases there were three, in which all the bile was draining through a cholecystostomy wound, with absolutely acholic stools. There was no indican in spite of the much-spoken-of "bile insufficiency."

Conspicuous was the indicanuria in several cases of ozena and caries of the teeth in patients who exhibited

no other signs of pathologic condition. Evidently the patients swallowed in their sleep more or less virulent pus which furnished the source of intestinal infection and putrefaction, the stomach being empty and not containing any hydrochloric acid.

I have endeavored to remove this indicanuria, which I have considered for these four years as only an indicator of intestinal putrefaction, by all means advocated heretofore: I have placed my patients on a vegetarian diet, mixed diet, proteid diet, lactofarinaceous diet. There appeared, however, no perceptible change in the excretion of indican in any one of the twenty cases of "intestinal antointoxication," I observed. I administered gelatin, lactic acid culture tablets, chlogestin, calomel, menthol, ichthoform, ichthalbin, benzonapthol, ichthyol, hydrochloric acid—without avail. I combined oil injections simultaneously with this internal and dietary treatment, and in another series of cases salicylic acid irrigations of the colon—all with no success whatever. I imported and used in many instances Metchnikoff's lactobacillin, with not the slightest reduction of indican in the urine. I used all makes of lactic tablets with which any manufacturer could supply me—but the "commercially so well-advocated antiputrefactive action exercised by lactic ferments, when applied to the treatment of intestinal disorders" proved a complete failure! Not the slightest influence on the excretion of indican in the urine could be seen from any of these preparations. At last I resorted to high enemas of 1 per cent. ichthyol with the patient in knee-chest position. I think the case in which I first applied the latter noteworthy enough to be reported.

A man aged 72 with pernicious anemia (the blood-picture showing poikilocytes, megalocytes and megaloblasts, the hemoglobin 30 per cent. (Sahli), red blood corpuscles 2,700,000) showed excessive indican for two weeks previous to the treatment. The physical examination of the body, and the examination of the feces, and

of the urine revealed nothing further. The patient was put on lactofarinaceous diet, combined with daily high colonic lavage with 1 per cent. ichthyol. The indican disappeared from the urine, and the blood increased in the course of four weeks from 30 to 65 per cent. (Sahli). The megaloblasts disappeared from the blood. The patient is at present much improved.

Startled by the efficiency of ichthyol irrigations, I advised the same treatment for another patient, a middle-aged woman with depressive neurasthenia symptoms, with no other clinical symptom but persistent indicanuria. The indican disappeared, and the patient's whole mental attitude at the same time brightened conspicuously.

While I am aware that two cases are not sufficient to allow of any further general deductions for the therapy of this rare disease "intestinal auto-intoxication" I thought them noteworthy enough—in view of my numerous therapeutic disappointments in the treatment of that disease—to report.

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ABSTRACT OF DISCUSSION

DR. DELANCEY ROCHESTER, Buffalo, N. Y.: I had a case of pernicious anemia in which the injections were used as described by Dr. Baar, with only slight temporary improvement. The patient finally died. Although the injections were used for a long time, indican did not appear from the urine. I do not agree that these patients with pernicious anemia can be cured, when these large quantities of indican appear in the urine, by washing out the bowels with these ichthyol injections. I think, however, that Dr. Baar's general observations are true. Indican is present in the urine in a large percentage of these cases, but it is not necessarily due to intestinal putrefaction. We certainly do not get relief by the employment of lactic acid bacilli used in any way, as in buttermilk, or lactic acid tablets.

DR. JUDSON DALAND, Philadelphia: As already stated, indican is non-toxic; but inasmuch as materials are manufactured during the process of putrefaction which are toxic, and as indican is an indication of their production, the presence of this substance in the urine may be of some value to us.

So far as pernicious anemia and the type of blood picture referred to is concerned, I also have had an interesting case. This experience was with a child about 12 months of age, who presented a persistent and excessive indicanuria. The colon was irrigated with normal saline solution, and this was followed by a rapid recovery. In this case certain materials remained in the blood and were active until destroyed, and we were able to recover from the urine cadaverin and putrescin. I believe that where there is an indicanuria which will not yield to treatment, often we will find tuberculous ulceration of the intestine, and also that any interference with the integrity of the intestinal canal will bring about indicanuria. Of course, the extent of the intoxication is exceedingly variable. I think the suggestion made as to the treatment of these cases is a valuable one; thorough and complete irrigation of the colon with normal saline solution should prove to be very efficient.

Dr. Jay I. Durand, Atlantic City, N. J.: During the last four years I have examined 5,000 specimens of urine, making the indican test as a routine measure. I have found indican, in definite amounts, in at least two-thirds of the specimens; if we accept the teachings that any trace of indican is pathologic, then at least two-thirds of the cases were pathologic. I agree with Dr. Baar regarding the difficulty in removing the excess of indican in a large number of cases. There are many cases in which I have been unable permanently to reduce the quantity; I have used Metchnikoff's bacilli, in many preparations, and have never been able to convince myself that they had a marked effect on the indicanuria. It seems to me that, if Metchnikoff's theory were to be substantiated, the indican should be profoundly affected by the use of the bacilli.

Dr. C. Shattinger, St. Louis: I should like to make a report of a case recently under my observation. This case was, and still is, a puzzle to me so far as a correct interpretation of the symptoms is concerned. The patient was a boy of 18 years and he had been ill for 2 years. The symptoms were somewhat vague—mainly abdominal pain and progressive emaciation. He had had an appendectomy, and had made a good recovery from the operation, but improved slowly. He afterward lapsed back again and the emaciation became extreme. When he came under my observation his weight was 79 pounds and he looked like a candidate for death from tuberculosis. The suspicion of a tuberculous lesion in the intestine was strong. The feces were examined for tubercle bacilli, but none were found. The von Pirquet test was twice negative. The blood was carefully examined. Except for a reduction of about 20 per cent. in hemoblobin the blood was found to be normal. All the organs were examined carefully, and with negative results. Examination of the urine showed it to be normal, except for the presence of indican in what

would be called considerable quantities. I took that as a clue and an endeavor was made to remove the indicanuria. I have had a similar experience as Dr. Durand in the use of the different medicinal agents and the bacillary preparations. I used all, but without avail. In the want of better indications I fell back on what seemed to be common sense view of the indications. I wanted to improve the nutritive condition of this patient, and so I fed him to the utmost. I felt that he should derive benefit from the employment of hydro-electric baths, viz., sinusoidal baths, to stimulate metabolism. By using hydrotherapeutic measures, tonics, salines and carefully selecting the diet, I found it was possible after 7 months to bring his weight up to 132 pounds and apparently to make him a strong and healthy individual. But he still has indicanuria.

Dr. Gustav Baar, Portland, Ore.: Intestinal toxemia is a very uncommon disease; among 3,000 cases examined there were only about twenty in which I could not find the cause for the constant presence of excessive indican in the urine. Where there was a renal, gastric or liver insufficiency I have not called such cases "intestinal" toxemia. I want to avoid the expression auto-intoxication; this is a term that should be avoided, as should the term malaria. I noticed that those who took part in the discussion agreed that the lactic acid tablets show no influence on the excretions of indican. If we need any such nostrums let us have something that is less expensive than these lactic acid tablets. Here is another point: the excessive secretion of indican in the urine occurs in cases of hyperacidity; this is something of diagnostic value. Cases of hyperacidity point more to the neurotic conditions, or ulcer of the stomach; cases of hyperacidity associated with persistent indicanuria, however, point to extragastric lesions (gall-stones or appendicitis), and they belong to the surgeon.

THE TREATMENT OF TYPHOID BACILLUS-CARRIERS

WITH REPORT OF A CASE TREATED BY INOCULATIONS OF TYPHOID VACCINE

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TYPHOID IMMUNITY

One year ago, before another Section of this Association,[1] I presented the results of a study of typhoid immunity and anti-typhoid inoculation. It was shown at that time that the factors of acquired immunity in typhoid were largely concerned with the process of phagocytosis, and those antibacterial elements which make phagocytosis possible; i. e., the opsonins and stimulins. The other antibacterial elements, the bacteriolysins, bactericidins and agglutinins, while possessed of certain powers antagonistic to the infection during and immediately subsequent to the attack, were considered, according to work so far done, of lesser value in the perpetuation of such immunity.

In this disease, as in many others accompanied by leukopenia, the problem of active immunization seems to resolve itself into a study of these measures which primarily augment the number of leukocytes, with secondary augmentation of those antitropic substances which render the leukocytes capable of phagocytosis.

After recovery from typhoid, as from certain other acute infections, the immunity acquired by the body

1. Stone, W. J.: Typhoid Immunity and Antityphoid Inoculation, THE JOURNAL A. M. A., Oct. 16, 1909, p. 1253.

cells usually lasts during the life-time of the individual. As shown, however, in the previous study, the immunity thus induced may vary greatly, and it is not at all uncommon to find that more than one undoubted attack has occurred within six or seven years. Dreschfeld's figures based on 2,000 cases in the Hamburg General Hospital showed that only 0.7 per cent. were affected twice. It is probable, however, that the incidence of multiple infection is greater than these figures indicate.

On the other hand, it must not be forgotten that other bacteria may produce conditions which are clinically identical with typhoid, and which many times are diagnosed as typhoid. The differentiation of typhoid-like, paratyphoid, colon and paracolon infections is by no means easy under the most favorable circumstances. Some types of meningitis and *Bacillus coli* septicemia may give positive Widal reactions in dilutions usually considered diagnostic of typhoid, and when made by an observer familiar with the motility of the strain. Lumbar puncture will, it is true, in most cases, clear up the diagnostic atmosphere in cases which are suspected to be typhoid but in which there are positive Babinski and Kernig's signs; while blood cultures, in septicemia due to the *Bacillus coli communis,* will usually give sufficient evidence for differentiation. Certain strains of *Bacillus coli,* however, may not produce indol or coagulate milk, and differentiation may be possible only after prolonged cultural and animal tests.

The virulence of the infection—a factor of importance, but, unfortunately, in our present state of knowledge, difficult to ascertain—undoubtedly has much to do with the problem of immunity; since, if overwhelming in one instance, little active immunity may result, while if mildly stimulating in another with good cellular resistance, an active, long-persisting immunity may follow. This is in accord with present knowledge

of all infections which produce their destructive results through growth and death of the bacterial cell within the body, i. e., by so-called "endotoxins." The problem is somewhat different in such infections as diphtheria, pneumonia or tetanus, which do their damage through toxins elaborated during the life of the bacterial cell. The efficient neutralization of these toxins, in all probability a purely chemical problem, is followed by recovery but not by an efficient immunity.

TYPHOID CARRIERS

One of the most interesting problems with which we are concerned in typhoid is in connection with typhoid carriers; i. e., the persistent elimination of bacilli for years after recovery, and during an interval when the individual shows increased resistive powers by methods calculated to measure his state of immunity. Such immunity, which may be designated as partial or incomplete immunity, is in all probability sufficient to protect the body cells against the damaging influence of the infection, but insufficient to exert any destructive or antagonistic power directed toward eradication of such infection. In other words, the phagocytic power may be higher than normal while the bacteriolytic and bactericidal powers may be low.[2]

In practically all reports of typhoid carriers, such individuals were not seriously inconvenienced by the presence of the infective agent which earlier, before partial immunity was established, produced manifestations of the disease. According to Park,[3] in most

2. The determination of the opsonic index in patients with acute typhoid infection is difficult, since the bacilli are susceptible to the agglutinative and bacteriolytic action of the serum. In chronic typhoid infection (carriers), after one year, the agglutinative and bacteriolytic effects are, as a rule, markedly diminished, and the determination of the opsonic power of the serum is a matter of less difficulty. This matter of the time element accounts for the discrepancy in the results obtained by various workers on different patients.

3. Park, W.: Typhoid Bacilli-Carriers, THE JOURNAL A. M. A., Sept. 19, 1908, p. 981.

chronic carriers, the bacilli are eliminated with the feces, while the urine contains the bacilli in a relatively smaller number.

Connell[4] regards the bile as the medium in which the bacilli perpetuate themselves. He regards the feces as a greater source of danger during the active stage of the disease, and the urine as the great spreader of the disease during the decline and post-febrile stage. Forster believes the gall-bladder to be the site of constant reproduction of the bacilli, which are intermittently ejected into the intestines; a view also held by the Ledinghams,[5] since investigations have shown that the bacilli may disappear during convalescence, only to reappear several months later.

Typhoid carriers who become such through association with the disease, "contact carriers"—and such instances are not uncommon among nurses and orderlies—who themselves have not had typhoid to their knowledge, likewise show tolerance to the presence of the germs without inconvenience. Their tolerance is probably to be explained as due either to a natural immunity or to partial immunity from an earlier unrecognized mild typhoid infection. From this standpoint it is not illogical to assume that the measure of immunity which protects the individual during and subsequent to attack against the infection itself, is to be found largely in those antitropic substances which are concerned with an augmented power of phagocytosis; while lowered antibacterial substances, such as the bacteriolysins and bactericidins, permit the infection to persist for years in the individual without serious damage to himself, but without eradication of the bacterial elements.

The history of typhoid carriers varies greatly. In most instances they have been discovered in hitherto unexplainable endemic outbreaks among the inmates of asylums or among families who have happened to em-

4. Connell, K.: Am. Jour. Med. Sc., 1909, cxxxvii, 637.
5. Ledingham, A. and J. C. G.: Brit. Med. Jour., Jan. 4, 1908.

ploy the same cook or obtained milk from a dairy previously under suspicion because of its possible connection with earlier endemics. A larger number of typhoid carriers, in the sense that they have been the cause of endemics, have been women who have in some way been connected with the preparation or handling of food products. Houston[6] in 1899 reported the first case of persistent typhoid bacilluria in a "contact" typhoid carrier, who for three years had shown symptoms of chronic cystitis. The largest number of recorded cases having origin from one source was reported by Lumsden and Woodward,[7] who found a typhoid carrier in a dairy responsible for fifty-four cases of the disease among the dairy customers.

The time since the original attack has varied from one to fifty-four years. Scheller,[8] who investigated an endemic on an estate in Prussia, found that during a period of fourteen years, thirty-two cases of typhoid had occurred, traceable to a woman employed in the dairy, whose attack had occurred seventeen years previously. Typhoid bacilli were found in her stools in almost pure culture. Out of forty people who drank of the milk of this dairy, eighteen were found to be typhoid carriers, and yet only five of the eighteen had ever had typhoid. Such individuals must be considered "contact carriers," as above mentioned.

Soper's most painstaking investigation[9] showed that in six years twenty-six cases of typhoid could be traced to a cook employed successively in households where the disease appeared. Typhoid bacilli were obtained from her stools; none were found in the urine; her blood gave positive agglutinative tests. The Leding-

6. Houston, T.: Brit. Med. Jour., Jan. 14, 1899.
7. Lumsden, L. L., and Woodward, W. C.: A Milk-Borne Outbreak of Typhoid Fever Traced to a Bacillus-Carrier, THE JOURNAL A. M. A., March 6, 1909, p. 749.
8. Scheller: Centralbl. f. Bakteriol., 1908, No. 5, p. 385; abstr. editorial, THE JOURNAL A. M. A., June 13, 1908, p. 1986.
9. Soper, G. A.: The Work of a Chronic Typhoid Germ Distributor, THE JOURNAL A. M. A., June 15, 1907, p. 2019.

hams,[5] in the course of a study of the inmates of a Scotch asylum where typhoid had been endemic, found thirty typhoid carriers out of a total of ninety women examined. Gregg[10] has reported the case of a boarding-house mistress who served as the source of infection in seven cases of typhoid fifty-two years after her own recovery. No bacilli were found in the blood or urine, but pure cultures were obtained from the feces. Jundell has described the conditions present in a family the mother of which was shown to be a typhoid carrier, over fifty years after her attack. During an interval of fifty-four years, twenty-two members of the family were attacked. This carrier was 83 years old and her feces were found to contain typhoid bacilli. Huggenberg[11] reported thirteen cases of typhoid in a family, traceable to the mother, whose attack had occurred thirty-one years previously, and whose feces contained the bacilli.

Park[3] has estimated that fully 2 or 3 per cent. of typhoid convalescents become chronic carriers, in the sense that the bacilli persist after years in stools and urine, and as such are dangerous to the community. Probably not more than one-half of such carriers actually infect others.

DIFFERENTIATION OF CHRONIC TYPHOID BACILLURIA FROM BACILLURIA DUE TO BACILLUS COLI COMMUNIS

Colon bacillus infections of the urinary bladder in women are relatively common for anatomic reasons. It has been found exceedingly difficult in my experience to differentiate some forms of bacilluria due to the bacillus coli from chronic typhoid bacilluria. At the present time, I have under treatment two cases in which the cultural methods are confusing. Neither individual to his knowledge, has had typhoid fever. Both were considered from the early cultural tests as "contact"

10. Gregg, D.: Boston Med. and Surg. Jour., July 16, 1908.
11. Huggenberg, E.: Corr.-Bl. f. schweiz. Aerzte, 1908, xix, 635.

typhoid carriers; but latterly, the same strains which in the beginning did not produce gas in glucose gelatin, or produce indol, or coagulate milk, have been found to do so in slight amount, and the earlier expressed opinions are open to question.

One may differentiate these cases, I believe, in another way, i. e., by the local reaction to injections of autogenous vaccine. The colon vaccine is much more toxic than typhoid vaccine, although occasionally one may meet a relatively non-toxic colon strain. As a rule, however, an injection of 50,000,000 colon bacilli produces a local reaction equivalent in intensity to a dosage of 300,000,000 of typhoid bacilli.

THE TYPHOID CARRIER PROBLEM

The typhoid carrier problem is a perplexing one, since in certain American cities, where for years the disease has been endemic with a consequent large number of unrecognized carriers, the installation of adequate filtration plants, while reducing the disease incidences, will not for years to come rid these municipalities of typhoid. Popular education seems to offer a partial solution of the problem. Patients convalescent from typhoid should understand that from 2 to 5 per cent. of those who have the disease harbor the bacilli in their gall-bladders, intestines and urinary tract, for periods of years, and under such conditions become a source of constant danger to others.

It will be obviously impossible to control any large percentage of typhoid convalescents by bacteriologic tests, but it will be possible for physicians to educate their patients and always to bear in mind the possible connection between the earlier attack and symptoms, sometimes slight, referable later to the gall-tract, to a slight urinary cystitis, to a recurring mild dysentery, or headaches supposed to have their origin in faulty metabolism. Segregation of individuals known to be chronic carriers may be regarded as practically impos-

sible. Since every typhoid patient requires the constant care of at least two, usually three individuals, it can readily be surmised that a large percentage of such attendants become "contact carriers" without themselves manifesting symptoms of the disease. Park has estimated that "probably one in every five hundred adults, who have never knowingly had typhoid fever, is a typhoid bacillus carrier."

TREATMENT

So-called urinary and intestinal antiseptics such as phenyl salicylate (salol), sodium phenolsulphonate and hexamethylenamin have been found to possess little value in the treatment of chronic typhoid infection. Treatment by autogenous or stock bacterial vaccines seems to offer more chance of success. It has been shown by the extensive work of Wright and Leishman and his co-workers that the bactericidal and bacteriolytic properties of the blood serum are augmented to a considerable degree by the injection of typhoid vaccine. As shown in my previous paper on this subject, the bactericidal substances are increased four or five-fold by inoculations of typhoid vaccine. The bacteriolytic substances are also increased so that, as a rule, the serums of inoculated subjects when diluted 1 to 10 and mixed with living typhoid bacilli, will cause either complete disappearance of the organisms or their reduction to amorphous masses.

A stock vaccine is quite as efficient as vaccine prepared from recently isolated autogenous strains.[12] On the other hand, for various reasons, it is probably better to use a vaccine prepared from the patient's organisms. Irvin and Houston[13] have reported disappearance of the

12. The immunizing potency of typhoid vaccine six months old is apt to be diminished. The best results are to be obtained with vaccine not over three months old. Care must be used not to overheat the vaccine in preparation, since overheating greatly impairs its immunizing properties. The thermal death point of most strains of typhoid bacilli is 53 C. Occasionally one may meet a more resistant strain.

13. Irvin, S. T. and Houston, T.: Lancet, London, Jan. 30, 1909.

infection by treatment with an autogenous vaccine in a patient who had contracted typhoid seven years previously. In the course of the seven years, six persons living in the same house as the patient, developed typhoid fever. After she came under treatment, urinary antiseptics were tried without avail for five weeks. She received during the following two months five injections in doses varying from 50,000,000 to 500,000,000, with disappearance of the infection.

REPORT OF A PATIENT TREATED BY INOCULATIONS OF TYPHOID VACCINE

Mrs. A. B. P., aged 34 years, was seen Nov. 19, 1909. She complained of more or less constant chilliness, malaise and fatigue, diffuse abdominal tenderness, with constipation and tenderness over the gall-bladder and liver, with occasional painful micturition. These symptoms followed an attack of typhoid fever of five weeks' duration, one year previously. The attack was unattended with complications. The examination revealed a moderate secondary anemia due to menorrhagia (hemoglobin 72 per cent., Dare, erythrocytes 3,140,000); temperature normal; tenderness on palpation over gall-bladder, and general abdominal tenderness and distention due to gas. The urine was slightly cloudy, contained few pus cells or epithelial elements; no albumin or sugar, but with marked indican reaction which was persistent.

The diagnosis made at this time was secondary anemia, due to menorrhagia and constipation with auto-intoxication. The patient improved under Blaud's mass with cascara. Potassium bicarbonate was prescribed for the bladder irritation. In December, 1909, the bladder irritation persisting, hexamethylenamin was prescribed (4 gm. daily) but without effect. In January, 1910, cultures taken from the urine revealed two types of organisms; both were motile, neither liquefied gelatin; but one, the preponderating type, corresponding to the typhoid group, did not produce indol, or acid in litmus gelatin, or coagulate milk, or produce gas in glucose gelatin; while the other, corresponding to the colon group, responded to these tests. The patient's blood gave a positive agglutinative reaction in one-half hour in dilution 1 to 20 with a stock typhoid culture, and agglutinated promptly in dilution 1 to 40, the organisms corresponding to the typhoid group present in the urine. The opsonic index was 2.3 while the bactericidal powers of the blood serum, using a dilution of 1

in 5, were found to be below normal. Since normal blood serum shows bactericidal power against the typhoid bacillus in a dilution of 1 in 10 it seems safe to assume lowered bactericidal properties in this particular serum. The bacteriolytic properties of the blood serum were lessened, since in dilution of 1 in 2 no effects were noticeable, other than agglutination, in two hours. Typhoid bacilli were not found in the stools. An autogenous vaccine was prepared from the typhoid organisms present in the urine. She received between February 11 and April 29 six injections in doses varying from 100,000,000 to 400,000,000. The typhoid organisms were no longer present on the plates after six injections, although since that time a few organisms, corresponding to the colon group, mentioned above, have been found. The patient is now under treatment with vaccine prepared from the colon group of organisms. Her blood on May 18, 1910, would agglutinate a stock typhoid culture in dilutions up to 1 in 100. Her subjective symptoms, such as the painful micturition and abdominal tenderness, disappeared after the third injection. The tenderness on palpation over the gall-bladder has also disappeared. The opsonic index has not been determined since the series of inoculations owing to the rapid increase in the agglutinative powers of the serum which, as mentioned above, interferes with the estimation of the index. The bactericidal powers have been increased during the inoculation, so that in dilution of 1 in 20 no colonies developed on the plates in twenty-four hours, after incubation of the serum dilution with a bouillon suspension for 15 minutes. The bacteriolytic power after the series of inoculations was increased so that in dilutions of 1 in 10 the bacilli were reduced to amorphous masses in two hours.

CONCLUSIONS

A survey of the literature citing typhoid carriers treated by bacterial inoculations, although few in number, appears to warrant the following conclusions:

1. The time element is an important factor in the reaction of susceptibility to inoculations of bacterial vaccines in typhoid carriers. Typhoid carriers, injected within a comparatively short time after their infection, will in all probability, receive more benefit from properly prepared autogenous vaccine than from any other known form of treatment.

2. "Contact carriers," who never to their knowledge have had typhoid, are more susceptible to the inoculations than carriers who have had a definite attack of this disease, and who are in all probability more immune.

3. Where the infection has persisted for years, it may be difficult to clear up the condition by bacterial inoculation. The effort should at least be made, since in the somewhat similar condition, chronic carriers of apparently non-virulent tubercle bacilli, the bacilli often disappear from the sputum during a course of inoculations of some one of the tubercle products.

4. The immunity manifested by typhoid carriers is in all probability a partial immunity in the sense that while these individuals are protected against the infection through an augmented phagocytic power held by their body cells, the antibacterial substances such as the bactericidins and lysins are lessened to a degree insufficient to exert any destructive power against the infection.

The Colton Building.

ABSTRACT OF DISCUSSION

Dr. John J. Buettner, Syracuse, N. Y.: I wish to report the case of a typhoid carrier in which there was given a history of a typhoid fever thirty years before; there was possibly a reinfection five years ago. The disease in this patient was discovered by accident. The patient had a persistent diarrhea, with blood in the stools. There was absolutely no evidence—no abdominal tenderness, no rise of temperature, absolutely nothing—to suggest the possibility of this being a case of typhoid fever. The stools were carefully examined and pure culture of the typhoid germ was discovered. The urine at this time gave a positive diazo reaction. The Widal reaction was positive. At no time did this patient show any rise of temperature whatever. In this case autogenous vaccine was used; five injections were made of from 25,000,000 to 1,000,000,000 dead bacteria. This was done between the months of December and February. Since then three examinations of the stools have been made very recently and there has been no reappearance of the typhoid bacilli in the stools.

Dr. James T. Terrill, Galveston, Texas: The question of typhoid fever carriers is, of course, an important one; and of exceeding interest and importance are the diagnosis of these conditions, and the identification of these typhoid carriers who are a menace to the communities in which they live. In the course in bacteriology given at the University of Texas, we experimented in the laboratory with the students, seeing if we could not get the Widal reaction from their own blood. We found that a large percentage of the students who had had typhoid fever at some time of their lives gave either a positive Widal reaction or a partial agglutination. I should say that one out of five of the men who had had typhoid gave these reactions. The question that has interested me most is, how many men who have had typhoid fever and who give a positive Widal reaction, are really typhoid carriers. The identification of the typhoid bacilli in the stools, especially when they are few in number, is difficult It seems to me that the laboratory workers should develop some more certain and simpler method for the identification of typhoid carriers. Dr. Stone's work should be carried further, that is, testing the bactericidal, or perhaps "typhocidal" would be a better and more proper term to use, property; this might give very valuable information.

I have had occasion to attempt the isolation of microscopic organisms found at the autopsy table; in a series of ten autopsies I found from none up to six different varieties; the autopsies were made less than four hours after death. In this series, there was one case in which I identified the the typhoid bacillus and the patient had at no time given any history of the disease, so far as the hospital records are concerned. I should like to say in parenthesis, however, that the histories of charity patients are extremely unreliable and not to be depended on. Here there were one, possibly two cases, out of ten autopsied at random in which the typhoid bacillus was found. I believe that the extermination of these typhoid carriers rests with the manner with which they are treated. These patients should not be allowed out of quarantine till the physician is sure that they are rid of the germs of typhoid from mouth to anus. These patients should not be turned loose to become a menace to the community, but should be handled in a scientific way until they are free from the typhoid germs.

Dr. Willard J. Stone, Toledo, Ohio; I should like to emphasize one feature included in my paper in regard to the problem of typhoid carriers in general. Dr. William H. Park of New York some years ago gave some statistics of interest; he estimated that fully one in every 500 adults in the United States, who had never had typhoid fever, was a typhoid carrier; I confess that this was a surprise to me. At the

same time I believe this statement of Dr. Park's to be correct. It should be remembered that every case of typhoid fever requires the more or less constant care of from 2 to 3 individuals during the course of the disease and the possibility of these individuals contracting the infection is very great. Many of them do not manifest symptoms of the disease but become, as mentioned in my paper, typhoid carriers by contact; *i. e.*, "contact carriers." I do not believe that we should necessarily say that because the blood serum of an individual agglutinates typhoid bacilli in low dilution, that it is significant. However if the agglutination persistently occurs in moderately high dilutions, 1 to 40, or 1 to 60, then they may have some diagnostic significance. We should be very careful about diagnosing so-called typhoid carriers without having obtained the bacilli in pure culture from the stools or from the urine.

THE RADICAL CURE OF MALARIA; ITS IMPORTANCE AND HOW IT IS ATTAINED

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Science has almost solved the problem of malaria in all its phases; but, despite our almost complete knowledge of the life-history of the malarial parasite both in man and in the mosquito, despite our familiarity with all the manifestations of the disease, and despite the fact that every physician knows that it is easily prevented and ordinarily yields to treatment, malaria, though decreasing in severity and frequency, continues as one of the most prevalent diseases in many localities of the United States, in some places its mortality rate amounting to 25 per cent. of the total number of deaths.[1]

According to the statistics obtained from the last census, the number of deaths from malaria in the United States in the year 1900 was 14,909. The following states showed the greatest mortality: Arkansas leading with 1,730; then Texas, with 1,331; Alabama, 1,055; Louisiana, 1,030; Georgia, 1,011; Tennessee, 987; Missouri, 965; Mississippi, 938; South Carolina, 749; North Carolina, 527; Illinois, 497; Virginia, 409; Indiana, 340; and New York, 308.[2] These statistics are of questionable value, since they are largely derived from informa-

1. Sutherland, H. L.: Gulf States Jour. Med. and Surg. and Jour. Southern Med. Assn., February, 1910.
2. Twelfth Census of the United States, Vital Statistics, 1900, i and ii.

tion obtained by the census enumerators in the rural districts, and no doubt many deaths reported from malaria were due to typhoid fever and other diseases. It should be remembered, however, that malaria as a complication of pregnancy and of a number of diseases, and as a cause of arteriosclerosis and nephritis, is responsible for many deaths which are ascribed to other causes. It would therefore seem that these statistics do not overestimate the number of lives sacrificed to this easily preventable and curable disease.

The simple statement of the number of deaths from malaria does not half tell the story of its ravages. Its expense to the people of the United States is appalling. It is estimated that malaria costs our nation from $50,000,000 to $100,000,000 annually.[3] Dr. Albert Woldert, of Tyler, Texas, after a careful study of the mortality and morbidity rates of Texas, estimates that malaria costs that state more than $5,000,000 per year.[4] Assuming that the United States census mortality rates are as correct for Missouri as for Texas, and that the morbidity rates are in the same ratio, malaria taxes the state of Missouri more than $3,000,000 annually.

MALARIA UNNECESSARY

The unnecessary burden of malaria can be relieved simply by radically curing those suffering from the disease, but, strange to relate, this most important point has been most neglected. Malaria can be entirely eradicated, in one year, in any community, without regard to the number of anophelines present, if every person having the disease will take quinin long enough to be completely cured.[5] It is man, and not the mosquito, that carries malaria through the winter, thus perpetuating the disease. Therefore, the most important measure in the

3. Harris, Seale: Prevention of Malaria, THE JOURNAL A. M. A., Oct. 9, 1909, p. 1162.
4. Woldert, A.: Malarial Fever, Its Expense to the People of Texas, Tr. Med. Assn. Texas, 1904, p. 37.
5. Koch: Zetschr. f. Hyg., May 22, 1903.

crusade against malaria is its radical cure, and it is this phase of the subject that I shall discuss.

The average physician does not regard malaria as a serious disease. He relieves the acute symptoms in a few days and when a patient dies of malaria he feels that the patient has neglected himself. It is in the most malarial regions that the disease is most lightly regarded. We should emphasize the seriousness of the disease and the importance of its radical cure.

The complications of malaria which result from our failure to cure our patients are responsible for more deaths than the acute and pernicious forms. The manifestations of malaria, like those of syphilis, are protean, and no organ in the body is exempt from its ravages. Its most marked effect is seen on the renal organs[6] and the vascular system.[7] As a consequence, in malarial regions, the general death-rate is high and the mortality from nephritis and the various forms of paralysis is inordinately increased.

While there is certainly no relationship between malaria and syphilis, and the etiology, histology and pathology of the two diseases are widely and essentially different, yet many of the clinical manifestations are analogous. I realize that it is an "odious comparison," but it is made to emphasize the importance of the prolonged treatment of malaria.

Malaria and syphilis are general or systemic diseases, the organisms and their toxins circulating in the blood; both are inoculable; they have a definite period of incubation; in the secondary stage of syphilis there may be a fever of a remittent type (I saw a case of syphilis in the secondary stage, with daily rise of fever to 103 to 105 F., in which a clinical diagnosis of typhoid or malaria was made, but the laboratory proved it to be syphilis); there

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6. Moore, J. F.: Nephritis in Malaria, Am. Med., Dec. 28, 1901.
7. Marchiafava and Bignami: Twentieth Century Practice of Medicine, William Wood & Company, New York, 1900.

may be skin manifestations in malaria;[8] the tendency to chronicity is marked in both, as well as the proneness to involvement of many different organs; there may be prolonged periods of latency in malaria as in syphilis; no two diseases produce more nearly similar or more serious effects on the vascular system and renal organs; malaria is sometimes a cause of ulcerative keratitis,[9] optic neuritis, the acute psychoses,[10] sclerosis of the cord,[11] and even progressive paralysis;[12] in both diseases we have drugs which are almost specific in their action, but in order to get the best results treatment in both diseases must be begun early and continued for a long period.

Relapses, which result directly from our failure to cure our patients, may occur as recrudescenses of the fever soon after acute symptoms, as exacerbations during the chronic course of the disease, or as distinct attacks during latency. Reinfections are usually relapses or recurrences.

Celli[13] regards a relapse in malaria as the recurrence of symptoms at any time within one year from July 1. Reinfections occur after one year. Undoubtedly relapses have been observed several years after infection, and reinfections may occur in less than a year, but Celli's rule is a safe one to follow. If we adopt this rule and keep records of our cases we shall find how few of our malarial patients we radically cure.

The world owes a debt of gratitude to Manson for his self-sacrificing work in studying malaria, and he is rightly regarded as one of our greatest authorities on the disease; yet even he did not cure the disease in himself when first infected. He allowed himself to be inoculated by infected anophelines on Sept. 10, 1900, and had a

8. Reissman: Am. Med., March 22, 1902.
9. Ellett, E. C.: Ophth. Rec., March, 1899.
10. Bondurant, E. D.: Unreported Cases, Mobile, Ala.
11. Spiller: Am. Jour. Med. Sc., December, 1900.
12. Marandon de Montel: Rev. de méd., Nov. 10, 1900.
13. Celli: La malaria secondo le nuovo ricerche, Rome.

relapse on May 30, 1901.[14] Authentic cases of relapse after three years of latency have been reported.[15]

There would be but little chronic malaria if the acute cases were cured, but there are to-day probably two or three million persons in the United States who are harboring malarial parasites. Headaches, neuralgias, neuritis,[10] gastric disturbances and acute diarrhea are among the most frequent symptoms of the chronic or "masked" forms. Indeed, malaria may simulate almost any disease. Craig[16] reported fourteen cases of malaria which had been diagnosed as pulmonary tuberculosis.

TREATMENT

All authorities agree that quinin is almost a specific in malaria, when treatment is begun early and continued long enough to eradicate the parasite from the system completely, though there are differences of opinion as to the time of administration, the dosage, and duration of treatment.

Given a patient in a hospital where his symptoms can be watched, and with competent microscopists who can make repeated daily examinations of the blood, the rule "no parasites, no quinin" is best; but, practically speaking, nine-tenths of the physicians, in the rural districts where malaria abounds, have not microscopes, or the time to make blood examinations; therefore the diagnosis must be made from the symptoms and quinin administered at once. In malarial districts it is a good rule, when in doubt, to give quinin and watch for symptoms of other diseases. Quinin does but little harm in any disease, and it may do a great deal of good in eliminating malaria, which may complicate and make more serious any other disease.

The microscope is not always a criterion as to chronic malaria, because undoubtedly the disease does exist with-

14. Manson: Brit. Med. Jour., July 13, 1901.
15. Ziemann: Mense's Handbuch der Tropen-Krankheiten. Leipzig, 1906.
16. Craig: Med. Rec., New York, Feb. 15, 1902.

out the presence of parasites in the peripheral circulation. Now, however, that we have, in most states, laboratories connected with our state boards of health, where examination of blood is made free, and many private laboratories, where specimens may be examined for a small fee, the physician who is not equipped with a microscope should carry a few slides at all times and get a specimen of blood from cases of suspected malaria immediately before beginning the administration of quinin. He can get a report in two or three days, by telegram in twenty-four hours, if the symptoms are urgent. The few doses of quinin given before the report is received cannot injure the patient, and if the parasites are present the drug should be continued until a cure is effected.

There are differences of opinion as to the most favorable time of the day to administer the quinin. Torti's, also called the Roman, method of giving one large dose, 15 or 20 grains, several hours before the expected paroxysm, based on the theory that the best effect of the quinin is obtained during sporulation, when the youngest forms are free in the blood-stream, has many followers in the South. Some of the older physicians still follow Sydenham's method of giving one or more large doses during the remission or intermission of the fever, when the drug is less apt to produce nausea or other discomfort. In my opinion the best method, that employed by Gorgas, Deaderick,[17] Craig,[18] Rogers[19] and other authorities, and the method which I have employed for fifteen years, is to keep the patient continuously under the influence of quinin, by giving him small doses every four hours, both day and night, with perhaps an extra dose about four hours before the expected paroxysm.

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17. Deaderick: A Practical Study of Malaria, W. B. Saunders Co., 1909, p. 366.
18. Craig: The Malarial Fevers, William Wood & Company, 1909, p. 377.
19. Leonard, Rogers: Fevers in the Tropics, Oxford University Press, 1909, p. 234.

In the tertian and quartan forms 3 or 4 grains every four hours is sufficient, but in the more resistant estivo-autumnal variety 5 grains every four hours will be required. This dosage should be kept up for three or four days after the fever has subsided; then half the quantity should be given for two weeks. I do not believe that there is ever any occasion for giving more than 30 grains of quinin a day, and the very large doses are regarded by some authorities as positively dangerous.

In the acute and severe estivo-autumnal fevers the quinin may have to be kept up in maximum doses (30 grains daily) for several weeks, because the crescents, or gametes, are very resistant to quinin. In 1904 I reported a case of a negro girl, aged 14, who had crescents in her blood after the administration of 4 grains of quinin, in solution, every four hours for twelve days.[20] Darling, of the Canal Zone, in the Section on Practice of Medicine last year reported a number of cases in which gametes remained in the blood from two weeks to twenty-five days in spite of the daily administration of 30 grains of quinin.[21] Craig has also made extensive studies of the gametes in the peripheral circulation for varying periods of time after the use of quinin.[22]

In the acute cases of all types of malaria it is important for the patient to remain in bed for several days, because undoubtedly the best effect is obtained from quinin while the patient is at rest.

How long should the quinin be continued to attain a radical cure? Deaderick[17] says: "A few days' treatment with quinin no more cures malaria than does a few weeks' rubbing with mercury cure syphilis." He continues the quinin in 15-grain doses on two successive days of each week for two or three months. Craig, Rogers

20. Harris, Seale: Therap. Gaz., Jan. 15, 1904.
21. Darling: Tr. Section on Pract. Med. A. M. A., 1909.
22. Craig, Charles F.: The Sexual Forms of the Malarial Plasmodia Occurring in the Blood of Man, Arch. Int. Med., April 15, 1910, p. 325.

and other well-known authors also advise a modification of Koch's method.

In Italy small daily doses (6 grains) are given for three months after the acute symptoms have subsided, just as it is given to entire communities for the prophylaxis of the disease.[23] No doubt the prophylactic doses effect cures in many chronic cases, since in some localities the disease has been almost entirely eradicated and in five years the Italian death-rate from malaria has been reduced three-fifths (Thayer).

Ross[24] says: "To extirpate the parasite in a patient demands four months' assiduous cinchonization," and I believe that this is the safest rule to follow.

Thayer advises the small daily dose (6 grains) rather than the large intermittent doses. My experience has been that the small daily doses (3 grains night and morning) are efficient and are better borne than the large doses repeated at intervals of several days. I have also found that the memory test of giving quinin on certain days of the week or month is too severe for malarial patients, and they frequently give it up in disgust, while by taking it two or three times a day they form the quinin habit and will keep up the drug for even longer periods than is desired.

PROPHYLAXIS

It is not my intention to suggest any less vigilance in destroying anopheles mosquitoes and their breeding-places, and I would urge that those measures be employed to the fullest extent possible. I do maintain, however, that the most important and the most practical measure, at this time, in the crusade against malaria, is the radical cure of those harboring the parasites, because every patient cured means one less focus of infection. We should remember that there are malaria carriers as well

23. Thayer: The Prophylaxis of Malaria, Jour. Southern Med. Assn., November, 1909.
24. Ross: Albutt's System of Medicine, p. 285.

as typhoid carriers, and that one is as dangerous to the community as the other. We should not forget that the patient with the parasites of malaria in his blood may infect mosquitoes and transmit the disease to others, just as in yellow fever, and that malaria may be as serious a disease as yellow fever.

I believe that we should at once institute a campaign against malaria. It offers the most brilliant results of any of the public health problems now confronting us.[25] A campaign of education should be begun with the medical profession, because physicians as a class, and particularly those residing in malarial regions, do not appreciate the seriousness of malaria, or the ease with which it may be eradicated. The public should be educated by means of popular addresses and literature on the subject should be placed in the hands of every one residing in malarial districts. Malaria, being both infectious and contagious, should be classed as among the reportable diseases, and the state and county boards of health should lead in the fight. Municipalities, counties and states should be called on to furnish money to purchase quinin to cure the indigent sufferers from malaria and to destroy the anophelines and their breeding-places. Philanthropists should be urged to aid in this fight against one of the greatest enemies to mankind. Money spent in eradicating malaria will yield greater returns than any other philanthropy.

It is no idle dream to hope that the blot of malaria may be erased from the fair name of our Southland and from the Mississippi and Missouri valleys, where the disease is most prevalent. Our government has given us an example of what may be accomplised even in the tropics. Gorgas,[26] with the resources of our great country to aid him, when he applied the knowledge of the mosquito

25. Harris, Seale: Some Problems in Medicine which Affect the Prosperity of the South, Jour. Southern Med. Assn., April, 1909.

26. Gorgas, W. C.: Malaria in the Tropics, THE JOURNAL A. M. A., May 12, 1906, p. 1416; Ann. Rep. Dept. of Sanitation, Isthmian Canal Commission, 1908, Government Printing Office, Washington.

transmission of disease and eradicated yellow fever and malaria from Havana and the Canal Zone, made conquests which should be regarded as among the greatest in the history of the world, victories that mean more for the welfare of nations than have ever been achieved in war.

ABSTRACT OF DISCUSSION

DR. CHARLES MACLELLAN, Chicago: In my opinion the theory of the anopheles being the only carrier of malaria is wrong; malaria is sometimes found in northern latitudes where there are no anopheles. I remember, while in the Orkney Islands, being called to see a sick man, suffering from a severe attack of malaria, and in that region mosquitoes are unknown. Of course the gnat, of the same genus, exists in the British Isles. A second case in a man who had never been off the island came to my knowledge. Of course, we know that the anopheles is the great carrier of malaria, but there must be a first cause in the mosquito region.

With regard to the method of treatment, the administration of quinin in capsule or powder, is not an efficient manner of getting at the disease for its eradication. I believe the best method of administering this agent is in a solution of sulphuric acid. I have in mind one patient who gave a history of malaria, having been ill over a week and who had taken from 6 to 10 grains of quinin in capsule 3 times a day, without result; on giving him 2 grains of quinin 3 times a day, of the solution just mentioned, he escaped the chill on the second day and it did not return.

DR. ARNOLD TRAUBITZ, Neelysville, Mo.: I live in a district where every patient who goes to a physician's office is supposed to have malaria, and, having treated many of them with success, I cannot agree entirely with the method of treatment just outlined. Giving quinin 3 times a day for 3, 4 or 5 months is wrong, the patients cannot stand this treatment because of the resulting gastric disturbances. My method of treatment of the malaria that shows itself every other day, or every third day, consists in giving 4 or 5 hours before the expected attack, in one dose, from 25 to 30 grains of quinin; I give this about 4 or 5 hours before the chill is expected. Even with such a dosage, often I do not get the results I expected. I have given as much as 60 grains at one time. I find then that the patient always misses the next chill. It should be remembered, however, that the chill cannot be broken on the same day that the quinin is administered. Some patients cannot stand quinin every 4 hours. The main thing in the treatment of this disease is elimination; the stomach must be in proper condition to eliminate and cause a proper action of the gall-bladder; otherwise patients must be

kept on quinin indefinitely, a procedure which they cannot stand. The long-continued use of quinin is unnecessary. In treating malaria, the digestive system should at first be placed in a receptive condition for the specific; after the administration of the quinin the anihilated bacteria should be excreted from the system.

Dr. W. E. Chapman, Sheboygan, Mich.: In 1902, I served as contract surgeon in the Philippines, and was called to treat many cases of malaria. In one very stubborn case, running over a period of several weeks, I kept increasing the dose in capsules until 70 grains were taken daily, vacillating in my diagnosis between malaria and typhoid fever, as the quinin did not influence the fever, and at last being assured of my diagnosis, I dissolved 150 grains of sulphate of quinin in a weak solution of hydrochloric acid, and gave it to the patient in 4½ hours. The next morning the man was free from fever, he had a beautiful eruption and was very deaf, but for the following 3 months, while he was under my care, he had no more chills or fever.

Dr. I. J. Wolf, Kansas City, Mo.: One thing to remember, and one that Dr. Harris laid stress on, was that malaria may assume the picture of almost any organic disease we know or can name. I remember one case of intermittent pneumonia which was due to the malarial parasite. I have in mind also another case in which the malaria parasite was responsible for an acute attack of enterocolitis in a baby during the summer months. The question at first arose: Was the trouble due to a faulty diet? I had just read an article on malaria in children and I suspected that something of this nature was the trouble. An examination of the blood showed that it was swarming with malarial parasites. The proper administration of quinin brought an end to this attack of enterocolitis. I do not believe that the treatment of malaria differs in any way from the treatment of any other disease. One should never have a stereotyped method of treatment of this, or any other, disease. One physician spoke of giving enormous doses of quinin, while another referred to the giving of small doses. Whether the dose of quinin should be large or small depends on the patient who is to receive the remedy. It is very important that the question of the total eradication of the disease should be borne in mind, as well as the immediate cure. One should not be satisfied with the production of the latent stage—but should only be satisfied with cure. Thousands of dollars have been spent on the eradication of the mosquito; if a fractional part of this money had been spent on the cure of the patient much good could have been attained. Without a malarial patient, the mosquito could not be a conveyer of this disease.

Dr. Vernon Blythe, Paducah, Ky.: One thing that has not been sufficiently discussed is the difficulty of diagnosis of

malaria from certain other fevers, especialy typhoid. I am of the opinion that the giving of quinin in typhoid, which is done so much, does harm. I think that when a definite quantity of quinin has been given to a patient suspected of having malaria, and in those cases in which there is a question in diagnosis between malaria and typhoid, and when the quinin has had little if any effect on the temperature, the amount should be cut down to the minimum. The use of quinin in typhoid I believe to be distinctly harmful, especially to the circulatory and nervous systems. This drug has little effect on the temperature of typhoid, and I wish to enter a protest against its use in treatment of this disease.

Dr. S. P. Child, Kansas City: As Dr. Harris has stated there is great confusion at times and great difficulty in making a positive diagnosis between malaria and typhoid because of the absence of findings in the peripheral circulation. Physicians in Kansas City get many cases of malaria from Missouri towns and elsewhere; these places have many mosquitoes; a large number of cases appear in children and these have proved to be mainly of the estivoautumnal type. Some cases, in which the frequent examination of the blood has shown the malarial parasites, have previously been diagnosed as pernicious anemia. In a period of six months at the Mercy Hospital in Kansas City, a hospital for children, we have had 7 cases of malaria, diagnosed by the blood findings, with one death. There was one case of typhoid fever during this period. Among these 7 cases there were 3 of the estivoautumnal type, and the blood findings were suggestive of pernicious anemia. It was found that small and repeated doses of quinin by mouth would not cause a destruction of the organisms; therefore, we resorted to hypodermic medication of a combination of urea and quinin hydrochlorate; in every instance, as was shown by the result, we were justified in resorting to regular and systematic hypodermic medication. Only in 2 instances were large doses required and then we gave up to 12 grains every 2 hours hypodermically, in the gluteal muscles. In no case did we produce true cinchonism. These patients should be watched for several months before it is announced that a positive cure has been obtained.

Dr. C. C. Bass, New Orleans: In my section of the country we see malaria every month and every year; the disease there appears in two varieties. I believe that there is an impression among almost all the physicians practicing in that section of the country, that of all the specifics in medicine, one that is nearly a specific as any is quinin in treatment of malaria. A second impression that prevails is that in every patient who has malaria to such an extent as to give symptoms the plasmodium can be demonstrated in the blood by the use of the microscope.

Dr. Joseph H. Pratt, Boston: Many of the conditions accompanying malarial infection should not be confused with the infection itself. Various diseases of the nervous system are frequently attributed to malaria on insufficient evidence. I recently saw a typical case of migraine in a patient from Illinois who had been treated for years for chronic malaria. A physician whom she consulted in Boston concurred in the diagnosis and on examination of her blood reported that it was "swarming with parasites." This patient now 30 years of age has not had chills or fever since childhood. When I examined her she was not anemic and the spleen could not be felt. There were no malarial parasites in the blood. Certainly a medical man must be thoroughly imbued with the false idea that all sorts of nervous disturbances may be the manifestations of malarial infection to regard for a period of ten years a case of migraine as one of malaria in a patient who did not present a single symptom that was characteristic of the latter disease. It is a common error for the inexperienced man to mistake malarial parasites for blood platelets in stained specimens. There is no doubt, that even at present, many physicians in all parts of the country mistake typhoid, tuberculosis, and septic conditions for malaria. Many base their diagnosis of malaria solely on the presence of chills and fever. I remember a striking case in which the error was not discovered until revealed by autopsy. The chart was typical of malarial fever. The paroxysms, consisting of chills, fever, and sweating recurred regularly. Large doses of quinin had been given and although the fever did not yield, the physician in charge held to his diagnosis of malaria. Autopsy showed a purulent thrombus which filled the portal vein. Such experiences as these teach two lessons. 1. We should awake to the truth, so clearly stated by Osler, Craig and others, that a fever which does not yield to small, repeated doses of quinin properly administered with the patient confined to his bed, is not malaria. 2. Blood examinations are of no value unless made by a competent person.

Dr. G. C. Smith, Boston: The idea of a man from Boston speaking on the subject of malaria seems strange, especially as there is so little of the disease in Massachusetts. I know how prevalent the disease is in the middle west and south, but we in the New England states do encounter an occasional case. We have some cases imported from the west and south, and some patients have appeared here who reported that they were cured of malaria. It has been my fortune to see many such cases in consultation. I can corroborate the remarks of Dr. Pratt. During the past year I distinctly remember 3 cases of pyelitis of chronic form which had been diagnosed as malaria, and 2 patients with suppurative disease of the gall-bladder which had been treated with quinin, under which the chills and fever had subsided. The patients were

supposed to be cured of the malaria. The attacks came and went. There was a repetition of the administration of quinin and always with the same results—temporary disappearance of the chills and fever. Of course the patients did not improve because of the quinin they took. I believe that there are so many suppurative affections which are liable to be misinterpreted as malaria, that this point should be emphasized.

Dr. J. A. Witherspoon, Nashville, Tenn.: I rise to insist on a never-ceasing effort on the part of the physician to teach people how to rid themselves of this fell destroyer. Notwithstanding the fact that our brothers in Boston may find cases in which errors in diagnosis have been made, such as pyelitis and infected gall-bladders, if they would only visit the delta of the Mississippi river they would have more respect for the old-fashioned malaria of which Dr. Harris has spoken. I will even go farther and say that we realize the mistakes that are made, and that blood counts are necessary, but from my own personal observation I believe that there is no better class of men who can handle malaria in general than those men who practice medicine in the south where this disease is so prevalent. It is a mistake to say that down there the diagnosis is made largely on hearsay and without proper examination. There was a time when, all over the country the physician looked at the patient's tongue and felt of the pulse and made a diagnosis; that is not true today in my section of the country. In spite of the statements made by Osler, Pratt and others that if a fever does not yield after administration of a few doses of quinin it is not malaria I wish to state that no more false statement was ever made in the Mississippi Valley than that; it certainly is not true. I agree with Dr. Harris that the early disappearance of the malarial plasmodium from the peripheral circulation in the latent cases of the disease does not mean that they are gone entirely from the circulation; one may repeatedly examine the blood and not find them; but they are still to be found in the deep-seated organs, lying there dormant, especially in the spleen and other organs. It requires several months of continuous treatment to eradicate the disease in such cases. It seems to be almost impossible to eradicate malaria of latent form if such patients are allowed to be up and around. We are up against a problem that costs not millions of dollars only, but hundreds of lives throughout the country because the disease is not properly treated in the latent stages.

Dr. C. Shattinger, St. Louis: The question in mistaken diagnosis from Boston is interesting, but I should like to bring up a reverse condition, and relate a case which occurred in Kentucky where malaria is so prevalent, and where physicians might be supposed to be familiar with the disease. This patient, a woman, suffered for a long period of time and it

was believed that she had some ovarian or uterine disease, and hysterectomy was decided on. By accident she happened to fall into my hands. Examination of the blood revealed swarms of the plasmodia. In this case 35 grains of quinin were given every 24 hours and it was necessary to keep this up for a period of 10 days before the paroxysms ceased. This corroborates Dr. Witherspoon's announcement that we cannot control the disease always by the administration of 1, 2 or 3 large doses of quinin.

Dr. R. Alexander Bate, Louisville, Ky.: A point brought out by Dr. Harris that impressed me very much was the quiesence of malaria for a period of 3 years. I do not wish to question this statement, but I wish that Dr. Harris would tell us why such a statement should be sustained. It is believed that the malarial protozoon segments in the light; therefore, this accounts for the immunity sustained by some of the negro race. I can readily understand why the protozoa might remain in a quiescent state for a reasonable period of time. But how can Dr. Harris explain that reinfection did not take place and that there was not a relapse? How can he explain or exclude the possibility of reinfection? It was suggested by one speaker that the malarial protozoa are in the deeper structures, not so much in the peripyheral circulation, and away from the light; but how can this be demonstrated?

It is of course beyond question that the mosquito is the active agent in the cause of malaria; but I think, with certain Italian observers, that the mosquito is not the only source of infection. In recent papers the statement has been made that we must eradicate the swamps before malaria can be eliminated from a district infected with this disease.

With regard to the periodicity of malaria, it should be remembered that there are many diseases of metabolism which show periodicity. Certain materials accumulate in the system unutil a period of toxicity is reached.

Dr. Arthur G. Bell, Dallas, Texas: A case in a blacksmith, weighing 250 pounds, in my district was diagnosed as hip-joint disease. He had been a confirmed invalid for several years, and simply directed the work at his shop. He told me that some physicians had diagnosed his case as rheumatism and that others had pronounced it hip-joint disease. One surgeon stated that the Y-ligament had been bound down by adhesions, and that nothing would give relief except an operation. I examined the man carefully. I decided that his facial expression indicated chronic malarial cachexia. He ridiculed the idea, giving no history of malarial complications. Nevertheless, I directed him to take 4 grains of quinin, 3 times daily, till an ounce had been taken. After this simple treatment had been continued for some time the trouble disappeared like magic. The ligaments soon assumed their nor-

mal actions. Frequently I have seen physicians who lived in the same state or county disputing vehemently whether it was right to give quinin in malarial hematuria or not. One says that if you give quinin in malarial hematuria the patient will die. The other says that if you don't give quinin the patient will die. Some communities would not tolerate a doctor if he gave quinin in such cases, and others would discredit a physician if he did not. The text-books agree no better than the practitioners. One says quinin. The other says no quinin. It is said, however, that in cases of malarial hematuria, in which there are red corpuscles in the urine, quinin is indicated whereas when there is hematin, or hemaglobin in the urine no quinin is safe. When I formerly took steps to stop the hemorrhage from the kidneys I usually signed an extra death certificate. I have not attempted to stop the hemorrhage from the kidneys in my late cases. I wish to call attention to the fact that in the disease called malarial hematuria there seem to lurk two distinct diseases —one demanding quinin and the other no quinin.

Will some one make the differentiation?

Dr. Isaac Ivan Lemann, New Orleans: One cannot be sure of his diagnosis of malaria without an examination of the blood for the plasmodium. This is a point that cannot be put too strongly. Dr. Harris is probably correct in looking on the incompletely treated patients as a reservoir for the further propagation of the disease. The plasmodia may be deep-seated in the internal organs, and not found in the peripheral circulation, but one can only determine that by aspirating, for instance, the spleen. Splenic puncture is relatively a rare procedure, and one which is not often justified. The real point I wish to make, however, is that in many of the cases of intermittent chills and fever the disease is not malaria at all; these might be the symptoms of a lot of other diseases.

Dr. B. W. Fontaine, Memphis, Tenn.: After an experience of ten years in a very malarial district it has become my rule to doubt the diagnosis of this disease, malaria, unless the parasite is demonstrated in the blood. After repeated search for the plasmodia in the blood, if I fail to find any, then I doubt the diagnosis of malaria.

Dr. J. A. Chilton, Van Buren, Mo.: My first experience with malaria was personal, having had it myself, and with ten years experience in wrestling with this disease as a physician, I have come to have certain fixed ideas regarding it, founded on this experience. I believe that the disease becomes dormant, so to speak, and remains deep-seated in the system for months, and that it requires in many cases months to free the system from it, and to effect a certain cure. I have treated a great many patients who would obtain

medicine enough to keep the chill off, and notwithstanding my advice to return for further treatment, would neglect the matter until another chill, or perhaps two, would send them back to me, usually some time for the fourteenth to the twenty-first day from the date of their first visit. I have had careless patients repeat this thing many times, thus demonstrating the necessity of continuous treatment. I wish to relate one case of interest. A young man, about 22 years old came to me for medicine to relieve his fever and headache temporarily. On inquiry and investigation I found him suffering from malarial chills, and he said that he had had them for about all his life, and almost constantly for the past two years and that he had "tried the doctors" till he was discouraged, and did not wish any treatment save to get temporary relief. This man's history, together with the clinical symptoms, were all that was necessary to establish a diagnosis. I succeeded in getting him sufficiently interested in his condition to agree to stay with the treatment for four months if necessary, which he did. After beginning treatment with quinin and other tonics as iron, etc., combined with sufficient elimination through the bowels, the man did not have another chill, and in two months the color came back to his cheeks, he regained his strength and was redeemed from the ravages of malaria;; he returned to his work, that of a common laborer. This man was under constant treatment for three months. I relate this case to illustrate the necessity of constant treatment, continued for a period of months, in order to cure malaria, and my belief that the plasmodium will "hibernate," so to speak, in the spleen for a winter, and come forth in the spring hungry and "seeking whom he may devour," resulting in another attack of chills, unless the patient be given proper and continuous treatment.

Dr. T. J. Ragsdale, Lee's Summit, Mo.: I should like to relate the history of four cases of malaria seen by me 2 years ago. These patients were four young men who had been away from town but returned to it with malaria. They were treated about three weeks and the malaria disappeared. These young men were apparently well from September or October until the following April. When all four developed chills and fever again within a week or ten days of each other. After three months of appropriate treatment they were cured. In citing these cases I wish to call attention to the regularity with which they suffered relapses.

Dr. D. C. Watt, Little Rock, Ark.: I dislike to think that the feeling against the mosquito is waning; the eradication of the mosquito is possible. Those of us who live and practice in the malarial countries know perfectly well that people who are protected from the mosquito by screens, suffer less from malaria than those who are exposed to the mosquito.

In the treatment of malaria I think the individual himself is very much neglected; we should treat the patient more than the disease; because if we understand the normal condition and abnormal relations, we will find that the plasmodia, will not be in evidence when the condition is practically restored to the normal. In the south most of the people carry with them the plasmodia; but what I wish particularly to emphasize is that we must pay more attention to the treatment of the individual. In giving quinin, a certain amount of discretion must be used. When I am treating patients from August to October I use very little quinin excepting as a prophylactic. But in the earlier months I give full doses to effect. I am sure that quinin has been the cause of immediate death of some of my patients suffering from subacute malaria. We have to consider the matter of waste and repair. I believe that it is the patient more than the disease that should be considered.

Dr. A. H. Vandivert, St. Joseph, Mo.: The statements in regard to the diagnosis of malaria by an examination of the blood, and the finding of the plasmodia, are correct, for this is the scientific way;; but in the larger percentage of the cases of malaria, the diagnosis will be made by other means than a blood examination. Frequently the diagnosis will be made on the symptomatology alone. We should be careful to differentiate between malaria, septic fevers and other forms of disease which cause periodical chills and fever. There is no doubt that the administration of quinin in proper doses, if properly assimilated, will eradicate the malarial poison. When giving quinin to the extent of ½ dram we are giving a sufficient amount to stop, temporarily at least, the malaria, or the malarial infection we come in contact with. If more than ½ dram of quinin is required it means that the quinin is not properly prepared, or that it is not the right preparation, and that the drug is not given in sufficient quantities. The question always is: Why is not the drug properly assimilated? If quinin is not taken up by the stomach, then it should be administered in some other way.

This whole question of malaria resolves itself, I believe, into the correct diagnosis by scientific means if possible, or otherwise by the clinical symptoms. Success in the treatment means the continuation of the treatment over a period of months, and looking to the proper assimilation of the agent which brings about the eradication of the malarial element from the system. This is the experience of most men who live in malarial districts and who are called on to treat this disease frequently. In my section of the country there is less malaria now than there was a few years ago; the draining of the swamps has caused a decrease in the number of cases. Malaria was very prevalent before the days of the investigation of the blood for the plasmodium. We certainly have advanced very far in our knowledge of this disease.

Dr. A. Comings Griffith, Kansas City, Mo.: I want to call attention to one point brought out in the paper, the similarity of malaria and syphilis. Recently a patient was brought to me with a history of infection, with chills and fever. Examination of the blood revealed the presence of the malarial parasite. This patient, a man, was placed on quinin in small doses and the chills and fever disappeared. However, the enlargement of the spleen and liver did not disappear. The patient got along nicely, was up and about, and 6 months later had shown no recurrence of the trouble. He went south because of some specific trouble and there the specific lesion was found. The blood again was examined but no plasmodia were found. The patient had a well-marked systolic murmur and his condition pointed to chronic endocarditis. He died. At autopsy there was found that the diagnosis was a correct one, chronic infectious endocarditis. There still existed an enlargement of the spleen and the malarial parasite in the blood.

Dr. Seale Harris, Mobile, Ala.: Regarding the administration of quinin in malaria, the ordinary soft gelatin capsule is usually easily dissolved in the stomach, but to be certain of solution, it may be followed with dilute hydrochloric acid. Most patients object to taking quinin in solution. Gastric disturbances following the administration of quinin do not often occur when the doses are small, but frequently follow the large doses, i. e. fifteen grains. Dr. Chapman spoke of giving a patient 150 grains of quinin in one day. His patient did not die but I think it dangerous to give such large doses. Large doses will not cure malaria any quicker, or more certainly than will 30 grains a day in divided doses. The experiments of Rogers in the tropics proved this. He gave as high as from 60 to 100 grains a day, but these large doses did not shorten the course of the disease any more than the 30 grains a day, and he found that the large doses were distinctly depressing.

Dr. Wolf mentioned a case of pneumonia supposed to result from malarial infection. Malaria may have been a complication but I do not think that the plasmodium can cause a true pneumonia. The presence of the parasite in the blood does not necessarily mean that the patient is not also suffering from other disease. Always look for something else. Dr. Bass's remarks regarding the frequent absence of the plasmodium in the peripheral circulation in chronic malaria I believe to be correct. Sometimes, however, we find the plasmodium in the blood of patients who give no history of having had chills, fever, or other acute manifestation of malaria. Dr. Pratt doubts that the malarial parasite causes neuralgia, neuritis, general paralysis and nephritis. One of my colleagues, Dr. E. D. Bondurant, who is professor of Neurology in the University of Alabama, has made frequent

examinations of blood of patients suffering from these diseases and other nervous disorders. He states that in the majority of such patients coming from malarial districts, malaria is the causative factor and the symptoms yield to quinin. Dr. Bondurant also states that he has seen cases of the acute psychoses due to malaria. Manson has also called attention to neuralgias and neuritis of malarial origin.

With regard to the effect of malaria on the kidneys, I merely cite the articles by Marchiafava and Celli in the "Twentieth Century Practice of Medicine," edition of 1900. Many others have also called attention to the fact that malaria may cause nephritis. It is unquestionable that arteriosclerosis is much more common in malarial districts than elsewhere. I must take issue with Dr. Pratt's statement about the cases of fever that do not yield to quinin in 3 days not being malaria. Most of them are not but some cases of malaria are very resistant to quinin. I must also differ with him in what he quoted Dr. Craig as saying. In the April *Archives of Internal Medicine*, Dr. Craig states that he found the parasite of malaria in the blood of a number of patients who had been taking quinin for varying periods of time, some of them longer than a week.

In 1903, in the *Therapeutic Gazette* I reported the case of a patient who had had quinin in solution in large doses for more than a week, yet the fever continued and crescents were found in the blood. Last year in this Section Dr. Darling reported several cases in which the patients had been given 30 grains of quinin a day for from 2 to 3 weeks yet the crescent forms were not destroyed. We all must agree with Dr. Witherspoon in what he says regarding the crusade against malaria. This is certainly very important and should hold the attention of all.

In regard to my authority for the long periods of quiescence or latency in malaria, I refer to Deaderick's book on malaria. Dr. Bate also spoke of the immunity, or infrequency, of malaria in the negro race. I do not believe there is any greater fallacy with regard to the negroes than is contained in such a statement. The statistics for 1900 show that in proportion to population three times as many negroes as whites died from malaria. The negroes certainly have malaria as much as do the whites but possibly not in so severe a form. I do not believe that there is any such thing as immunity to malaria. I agree with Dr. Lemann that a blood examination, whenever possible, should be made in every case of suspected malaria; but there are thousands of physicians all over this country who do not possess a microscope and yet who in nine-tenths of the cases are able to make a correct diagnosis of malaria. This is especially true in malarial districts. However, one should bear in mind that if a patient residing in a malarial district has a chill, it is

not necessarily due to malaria; it may be due to a number of other causes.

The real and important point which I desire to emphasize is this: If you do not question your diagnosis of malaria, give the patient quinin at once and keep on giving him quinin until he is radically cured. It has been proved that malaria can be absolutely eradicated from malarial localities by the use of quinin alone. Koch advanced this theory ten years ago, and his plan was carried out on some islands off the coast of Africa. In less than two years, by administering quinin, the disease was practically eradicated from them. In Italy and in southern Austria the same results were obtained. The most important point to remember in prophylaxis, is to cure malarial patients. Cure them. It takes several months to do this. But if you do not cure them they will be carriers of the infection from one year to another.

THE VISCERAL ANESTHESIAS OF TABES DORSALIS IN RELATION TO THE DIAGNOSIS OF ACUTE INFLAMMATORY CONDITIONS IN THE ABDOMEN

WITH AN ILLUSTRATIVE CASE

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The value of pain as an element of safety in the body economy and the disastrous effects of the absence of the normal sensibility of a part are illustrated in the destructive ophthalmia which so frequently follows a lesion of the trigeminal nerve, and in the familiar "Charcot joint" of tabes. Although trophic disturbances probably have some part in the development of both of these conditions the absence of the normal sensibility seems to play an important rôle in determining the progressive and destructive character of both processes. Slight injuries pass unfelt and unheeded. In the case of the tabetic arthropathy the absence of pain results in the absence of all reflex protective contraction of the muscles controlling the joint movements; the continued free use of the limb increases constantly the existing damage and there ensues a gradual, painless disintegration and destruction of the joint. A recent experience has brought home to me the fact that sensory disturbances in tabes may, indirectly, lead to grave damage to the body in ways other than by the development of "Charcot joints" or perforating ulcers of the foot. The following case illustrates this fact:

FATAL PERFORATIVE APPENDICITIS IN A TABETIC WITH COMPLETE ABSENCE OF PAIN, TENDERNESS AND MUSCULAR RIGIDITY

Patient.—A brakeman, aged 42, was admitted to the medical service of the New York Hospital on August 14, 1909, with an acute febrile attack of three days' standing. His history as given at that time was as follows: Family history is unimportant. The patient had measles in childhood; malarial fever twenty years ago; chancre seventeen years ago; treatment for a few weeks only; indefinite secondary symptoms; gonorrhea twice; last time four years ago. He was a heavy drinker up to eight years ago; since then has used no alcohol. For the past year has had some difficulty in controlling his bladder and rectum and has had frequent sharp, darting pains in the legs. About four weeks ago he began to have a "weak, tired feeling" in the legs; could not feel distinctly with his feet and would stumble when attempting to walk in the dark. Three days ago he began to be very feverish. Since then he has had several shaking chills and some profuse sweats. There has been no regularity in the appearance of the chills; no pain; no other symptoms except prostration and malaise.

Physical Examination.—Male subject, large frame, poorly nourished. Skin and mucous membranes of good color. Admission temperature 104.6 F., respiration 24, pulse 108.

Eyes: Left pupil smaller than right. No reaction to light in either pupil. Prompt reaction in accommodation. Tongue moist and clean. Superficial lymph-nodes not enlarged.

Pulses: Equal, regular, rapid, of good size and force, moderate tension. Arterial walls slightly thickened.

Heart: Apical impulse diffuse. Seen and felt in fourth and fifth intercostal space 13 to 14 cm. to left of mid-line. Right border of relative dulness not satisfactorily determined; left border 13 cm. to left of mid-line. Heart sounds clear except at apex, where a short, soft systolic murmur is heard.

Lungs: Percussion gives everywhere a somewhat short, "wooden" resonance. Lungs voluminous. Respiratory murmur is everywhere vesicular. No adventitious sounds.

Abdomen: Flat, soft, thin-walled. No rose spots. Liver dulness extends from sixth intercostal space to free border of ribs. Edge of spleen can be indistinctly felt just above the costal border. In the right iliac fossa a soft, elastic, elongated and freely movable mass (cecum?) can be distinctly felt through the soft, relaxed, abdominal wall. In the left iliac fossa a similar, somewhat smaller object can be felt. Neither mass is tender on palpation. No tender points can be elicited

anywhere in the abdomen, nor is there anywhere muscular rigidity.

Genitals: Small scar on glans.

Extremities: A number of pigmented, depressed scars over both shins. Knee-jerks and Achilles jerks cannot be elicited. Plantar reflex absent. Marked diminution in tactile and pain sensibility over feet and legs.

Course of Disease.—On August 15 the patient vomited several times. The temperature continued high and irregular. The mind was clear. The patient complained only of the fever and general malaise; required catheterization. Urine contained a trace of albumin and a good many hyaline and granular casts but no pus. Leukocytes were 9,700; polymorphonuclear cells 83 per cent.; lymphocytes 17 per cent.; hemoglobin 85 per cent. The Widal test was negative. There were no malarial plasmodia. The abdomen was soft, flat and entirely free from tenderness.

During the next six days the patient's condition grew slowly but steadily worse. The temperature fluctuated between 100 and 104 F.; the respirations between 24 and 32, and the pulse gradually grew more rapid and feeble. The patient continued to vomit frequently, the vomited matter consisting usually of bile-stained fluid. The bowels were readily moved by laxatives or enemas. The patient complained of no pain whatever, and frequent examinations of his lungs, heart and abdomen failed to supply any clue to the diagnosis. The Widal test was repeatedly negative. Two examinations of the scanty sputum failed to reveal tubercle bacilli. The urine gave no evidence of a pyelitis or cystitis. The soft elastic mass in the right iliac fossa seemed rather to diminish in size, could be readily displaced under the finger and was never tender to pressure or manipulation. It seemed to be only the normal cecum felt through an unusually thin and relaxed abdominal wall.

The stomach contents, expressed after an Ewald test breakfast, showed nothing abnormal. Examination of the stools was negative for blood, mucus or ova. Rectal examination revealed nothing abnormal.

On August 17 the leukocytes numbered 18,800 and the percentage of polymorphonuclear cells was 83. A blood culture taken on this day remained sterile. On August 20, the leukocytes were 37,800 and the polymorphonuclears 92 per cent. The abdomen at this time was somewhat tympanitic but was free from muscular rigidity and tenderness. The area of liver dulness remained unchanged. The heart sounds also had not changed. A few crackling râles could be heard at the bases of both lungs; the tongue was dry and brown.

It was evident that the patient was suffering from some severe septic condition but the nature and site of the trouble was still altogether obscure.

August 21, the patient failed rapidly, passed into a stupor, developed pulmonary edema and died at 9 p. m. In the light of the subsequent autopsy findings it is to be regretted that a systematic examination of the sensibility of the trunk should not have been made, but our attention was centered on the acute, febrile condition which seemed to be quite unrelated to the antecedent tabes.

Autopsy.—Fifteen hours after death. Dr. Symmers (condensed report). On opening the peritoneum about 500 c.c. of milky fluid escaped. The peritoneum is diffusely opaque, swollen, edematous and in many places covered with an abundant fibrinous exudate. The serosa of the intestines is opaque and the intestines are in many places matted together by fibrinous exudate. In the appendix a round perforation, the size of a 10-cent piece, is found. The edges of this are necrotic and covered with fibrinous exudate. A probe passes directly into the lumen of the appendix, the mucous membrane of which is necrotic and discolored.

Pleura and pericardium normal.

The heart is moderately increased in size and flabby. The endocardium is in good condition. The aorta is large, the intima presents many yellowish plaques alternating with pale, hyaline, wrinkled areas. Heart muscle shows post-mortem changes.

The lungs show only emphysema and edema.

The spleen is increased in size, soft and friable. The Malpighian bodies are not visible.

The kidneys are moderately increased in size. The capsule is thin, strips readily and leaves a smooth, pale surface. Cortex and medulla are well differentiated. Cortex is broad, swollen, opaque. Markings very indistinct.

Liver considerably increased in size. Cut surface smooth, yellowish in color and very friable. Markings indistinct.

Stomach presents the lesions of atrophic gastritis.

Intestines show little change.

Bladder and prostate fairly normal.

The spinal cord shows considerable grayish discoloration, involving the posterior and lateral tracts, which is chiefly confined to the dorsal region.

Microscopic Examination (Dr. Schlapp).—From the sacral region up into the upper part of the dorsal there is a very marked degeneration involving practically the whole of the posterior columns, showing that the root zones in the dorsal

region were involved as well as those in the lumbar and sacral region. The fibers in the cornucommissural tract are partly normal as are also a few fibers in the root zones. The root zones and the column of Burdach are intact in the cervical region. In both of Clark's columns the fibers are missing. On one side of the cord most of the cells are missing and those that are present show an abnormal condition in that they are very much smaller than is the normal cell in Clark's column. The cell-body has shrunken, the nucleus has also shrunken and most of the cells in both of Clark's columns contain a large amount of pigment. The cells in the anterior horn seem to be normal except that they contain quite an amount of pigment. The fibers in the posterior nerve-roots are almost entirely degenerated. The anterior nerve-roots throughout the sections of the cord are normal with the exception of a small bundle on each side which shows a marked degeneration. This degeneration, however, is sharply confined to this small bundle of fibers. The lesion extends up to the nucleus of Goll and Burdach, confining itself more or less to the column of Goll in the cervical region.

Here, then, was a man in good health, except for the rather mild symptoms of tabes, in whom an acute appendicitis developed, progressed to perforation and a diffuse peritonitis and ended in death, without there having been at any time spontaneous pain, tenderness or protective muscular rigidity.

Instances of the almost complete absence of these three symptoms in the peritonitis which follows the perforation of a typhoid ulcer are not very rare, but they occur only in patients showing profound prostration and apathy as a result of the severe intoxication of the primary disease. In the present case, on the other hand. the appendicitis developed in a man in his usual health and with an alert mind and a clear sensorium. Under these circumstances it can hardly be doubted that the explanation for the absence of these three cardinal symptoms must be sought in the sensory disturbances of the tabes.

DISTURBANCES OF VISCERAL SENSIBILITY IN TABES

Disturbances of visceral sensibility in tabes manifest themselves in (1) the well-known painful "crises" of the

stomach, intestines, bladder, larynx, heart, etc., and (2) a loss or diminution of the normal sensibility of certain of the viscera.

That such organs as the bladder, urethra, rectum and testicle may sometimes become anesthetic or analgesic has long been recognized. Gowers,[1] writing twenty-five years ago, notes the occasional loss of testicular pain, and adds that "the anesthesia may extend to the viscera when the trunk is involved. In consequence of the loss of sensation grave injuries to the limbs, such as burns, may be unperceived, and visceral disease may be unattended with the customary pain. Pleurisy, for instance, may be absolutely painless."

In recent years the subject of visceral anesthesia in tabes has received much attention from the French writers. It has been shown that complete anesthesia of both testicles occurs in about half of the cases and incomplete anesthesia in many more.

Normally, deep pressure or blows on the epigastrium cause a peculiar, painful sensation, with distress, collapse and sometimes even death. In about 20 per cent. of the cases examined this sensitiveness was completely lost.

In many cases there is a disappearance of the pain and distress usually produced by deep pressure on the trachea.

The pain occasioned by pressure on the globe of the eye and on the mamma is also frequently lacking.

Carrez,[2] who has reviewed the whole subject of the visceral anesthesia in tabes, concludes (1) that there exists no connection between the enfeeblement or abolition of the deep sensibility, testicular, mammary, epigastric, tracheal, ocular; and the superficial analgesia or anesthesia and (2) that there is no necessary relation between the deep analgesias and preexisting painful crises.

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1. Gowers: Diseases of the Nervous System, 1, edition 3, p. 454.
2. Etude clinique de quelques analgésies viscérales profondes dans le tabes, Thesis, Paris, 1903.

Although it seems clearly established that in locomotor ataxia there is frequently a complete loss of the normal painful response to irritation of certain of the viscera, the mechanism by which, under normal conditions, visceral pain is produced is by no means well understood.

It is a fact familiar to physiologists and surgeons (see Lennander[3]) that such organs as the heart, stomach, intestines, liver, gall-bladder, uterus, etc., are usually entirely insensitive to procedures (cutting, pinching, burning, etc.) which in the superficial tissues would cause severe pain; and it has always been difficult to harmonize this fact with the every-day experience that in disorders of these viscera pain is a common symptom. Mackenzie[4] has recently offered a hypothesis to explain this paradox, and supports it by many interesting facts. He believes that the pain excited by disturbances in the viscera is due, not to the propagation of true sensory impulses from the viscera themselves, but to the reflex stimulation of the cerebrospinal nerves supplying the tissues overlying these viscera; in other words, that the pain and tenderness are felt, not in the organ itself, but in the tissues of the thoracic or abdominal wall over it. Afferent impulses passing from the viscus along the sympathetic fibers to the cells of the spinal cord excite there the neighboring centers of the sensory and other cerebrospinal nerves. "If a morbid process in a viscus gives rise to an increased stimulus of the nerves passing from the viscus to the spinal cord, this increased stimulation affects neighboring centers, and so stimulates sensory, motor and other nerves that issue from this part of the cord. Such stimulation of a sensory nerve will result in the production of pain referred to the peripheral distribution of the nerve whose spinal center is stimulated, so that visceral pain is really a viscero-

3. Observations on the Sensibility of the Abdominal Cavity, Translated by Baker, London, 1903.
4. Symptoms and Their Interpretation, London, 1909.

sensory reflex. If the increased stimulation affects a motor center, then a contraction of a skeletal muscle results, and thus is produced the viscero-motor reflex."

This view of the nature of the pain excited by visceral irritation accords well with the familiar facts that such pain is often felt far beyond the boundries of the affected organ, and that there is often an associated hyperesthesia or tenderness of the skin and underlying tissues. In angina pectoris, for example, not only is the pain often felt in one or both arms but there is frequently also hyperesthesia of the chest wall and of the inner surface of the painful arm.

If this theory of the nature of visceral pain is correct (and there is much evidence to support such a view) it is obvious that the absence, in tabes, of the normal painful response to visceral irritation might be explained by assuming a destruction either of the sympathetic fibers bearing the afferent impulses from the viscera to the spinal cord, or of the spinal centers of the corresponding sensory cerebrospinal nerves. In the case cited here a lesion of the sensory cells of the cord alone would not, indeed, account for the conspicuous absence of muscular rigidity.

A lesion of the sympathetic fibers with interruption of the afferent impulses to the cord would, however, explain the absence both of sensory symptoms and of the reflex muscular rigidity. Is there evidence that such lesions of the sympathetic fibers occur in tabes?

LESIONS OF THE SYMPATHETIC IN TABES

Little was known concerning the condition of the sympathetic system in tabes until Roux,[5] in 1900, published his investigations on that subject. In all of the seven cases of tabes examined he found atrophy of a large proportion of the small myeline fibers in the cervical, thoracic and abdominal sympathetic trunks,

5. Les lésions du système grand sympathétique dans le tabes et leur rapport avec les troubles de la sensibilité viscérale, Thesis, Paris, 1900.

whereas in ten subjects dead from various other diseases no such changes could be found. He believes that he is justified in concluding that this destruction of the small myeline fibers is a special pathologic condition of tabes, and that this lesion is responsible for the disturbances of visceral sensibility in that disease. In this view he has the support of Déjerine and Thomas.[6]

In the case recorded here no examination of the sympathetic system was made.

Whatever may be the true cause of the disappearance of visceral sensibility in certain cases of tabes, the fact that such visceral anesthesia does sometimes occur seems to be well established. That this fact has a practical application is evidenced by the fate of the patient under consideration, whose life was lost because of the failure to recognize an acute inflammatory process in the abdomen, demanding immediate surgical relief, which under ordinary conditions would have been only too obvious.

Concerning the frequency with which the abdominal viscera, in tabes, lose their normal, painful response to visceral irritation we have at present no data. It is known that complete loss of testicular pain is found in about half of the cases and a loss of "epigastric sensibility" in 20 per cent. or more. If the lesions of the sympathetic trunks found by Roux are as frequent as his investigations seem to indicate, it is not unlikely that disturbances of visceral sensibility in tabes may be much more common than has been supposed.

Concerning the means of recognition of such anesthesia of the abdominal viscera little can be said. Carrez concludes that there is no relation between the disturbances of visceral sensibility and of that of the overlying skin. The absence of testicular pain and of that produced by deep pressure on the epigastrium would at least suggest that there might be similar sensory disturbances in the abdominal viscera.

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6. Maladies de la moelle épinière, Nouv. traité de méd. et de thérap., 1909, xxxiv, 588.

SUMMARY

The purpose of this report is to direct attention to the fact that in locomotor ataxia a loss of the normal sensibility of the viscera sometimes occurs, and that in such cases acute inflammatory diseases of the abdomen, such as appendicitis or peritonitis, may develop and run their course without at any time presenting any of the three symptoms of pain, tenderness and muscular rigidity. The loss of painful response to visceral irritation in tabes probably depends on a lesion of certain of the sympathetic fibers passing between the affected viscera and the spinal cord.

53 East Forty-Ninth Street.

ABSTRACT OF DISCUSSION

DR. LAWRENCE LITCHFIELD, Pittsburg, Pa.: I should like to ask Dr. Conner whether there was distention of the abdomen in the later stages of the man's illness, and, further, I should like to emphasize the point which he did not bring out sufficiently, that there was no relation between the superficial sensory nerves and those of the deeper structures. Within the past week I have seen a case of Pott's fracture in a tabetic, a man about forty-two years old, a syphilitic, who had been walking on his broken leg apparently for about two weeks before seeking advice. He had no anesthesia of his feet, he had no analgesia, he had barely appreciable hypalgesia of feet and limbs. He had good joint sense. Manipulation of the fragments elicited no pain. There was excessive swelling, which subsided after rest, with the application of icebags, after which the fragments were brought into alignment without the slightest sensation of pain.

DR. JOHN H. MUSSER, Philadelphia: It is one of the tragedies of appendicitis that it may frequently occur without either pain or tenderness or reflex spasm, and I have observed, in common with others, absence of these phenomena. Certainly, I have seen a number of these cases in various periods of life that I feel bound to say were not attended by or accompanied by locomotor ataxia. I am not stating this to disprove the statement of the author of the paper. I merely wish to emphasize the fact that these symptoms may be absent, and particularly is this the case in the gangrenous forms of appendicitis, in which, on account of the intensity of the infective agent, there has been an absolute cut-off of the nerve paths, consequently bringing about an absence of tenderness and an absence of reflex spasm. The one case

that comes to my mind at the present time is that of a healthy adult who had various attacks. At first, the usual preliminary characteristics of slight gastro-intestinal disorder ensued, with vomiting, some slight distention, a little pain, slight fever and then disappearance of symptoms in forty-eight or sixty hours, no abdominal reflexes, no tenderness, no pain. The man was quite an athlete and amused himself by contracting his own abdominal muscles in order to show us that he was absolutely free from pain. Notwithstanding the fact that we urged operative procedures, he refused until the onset of symptoms of peritonitis in two or three days, which were then characteristic. The toxemia was sufficient to carry him off inside of forty-eight hours, notwithstanding the fact that we had an operation and found that he had a gangrenous appendicitis. The only serious symptom that he had was that due to distention of the abdomen. Of course, the peritonitis was recognized by the other phenomena of disease.

Dr. C. F. Hoover, Cleveland: The dissociation of sensory percepts in tabes brought out by Dr. Litchfield, recalls to me a similar experience with a patient with Pott's fracture which was perfectly painless. The man could perceive the vibration of the tuning fork perfectly well. If the fragments were rubbed together he would say "I can feel a grating, but can feel no pain."

Dr. Lewis A. Conner, New York: The patient had, in the last two or three days of his illness, moderate distention, although the abdomen still remained soft. Of course, as Dr. Musser says, cases of appendicitis do sometimes occur, especially in children, in which the usual symptoms of pain, tenderness and muscular rigidity are almost entirely lacking; but, in my experience at least, some one or other of these symptoms has always appeared at some time in the course of the disease. In the case under discussion, it was the complete absence of these symptoms throughout the entire illness that made it seem so remarkable.

CERTAIN POPULAR BUT ERRONEOUS NOTIONS CONCERNING ANGINA PECTORIS

JAMES B. HERRICK, M.D.
CHICAGO

Severe substernal pain coming on after exertion, radiating to the left arm, lasting a brief moment, yet compelling the patient to remain immobile from the physical suffering and from a mental anguish that overwhelms him with a sense of imminent death—this picture is looked on by all as that of typical, true, cardiovascular angina, and especially when the arteries are found to be sclerotic and the blood-pressure high. A prognosis is made of sudden death in the near future from a recurrence of the paroxysm, a prediction only too often correct.

So indelibly is this image of the phenomena and course of the affection fixed in the minds of many physicians that they are unable to admit any deviation from its details as consistent with this disease. In this way there have become prevalent several notions concerning angina pectoris that are more or less erroneous, chiefly in that they fail to recognize the atypical manifestations.

It is the object of this paper to present some of these views that seem to me erroneous, chiefly because they are too narrow and do not give room for the exceptional case.

Considering the lack of definite unifying knowledge of the pathogenesis of angina pectoris, one is not surprised to find that there is confusion in the interpretation of the symptom-complex. This confusion is seen especially when the attempt is made to separate an

organic cardiovascular form from a toxic or from a neurotic type. I have no intention to discuss the necessity or advisability of making such a distinction, but shall limit what I say to the so-called "true angina" of organic cardiovascular origin. This tacitly assumes that a grouping of somewhat similar symptoms on a purely neurotic basis, no matter how closely resembling true angina, is not the real disease; that to this unreal disease the term "neurotic angina" or "pseudo-angina" is not inapplicable. In taking this position one realizes a certain inconsistency in the use of terms, and that one is open to the charge of not being in line with the latest trend of thought, of being at variance with the views of many leading medical men, and of exposing oneself to the shafts of ridicule of such a master of physic and English as Sir Clifford Allbutt. "Either a case is angina or not angina," says MacKenzie. "Pseudo-angina is pseudodiagnosis," says Allbutt. With all of which I agree, but feel that a clinical distinction between true and false is justified on practical grounds.

DEMONSTRABLE ARTERIOSCLEROSIS, HIGH BLOOD-PRESSURE, AND AORTIC VALVE LESIONS

Since Jenner proved that John Hunter, who died of angina, had coronary sclerosis, the conception of coronary sclerosis as the essential underlying lesion has been deeply rooted. That coronary sclerosis is often associated with sclerotic aorta, roughened aortic valves and wide-spread arteriosclerosis is also well known. From this frequent association has arisen the expectation of finding in all cases of angina evidences of this wide-spread arterial change, with its accompanying high blood-pressure and cardiac hypertrophy. But this, as has been pointed out by many, is by no means always the fact. Arterial change may be wide-spread and the coronaries sclerotic, yet there may be no hypertrophy of the heart and no rise in blood-pressure, the very sclerosis that is probably the cause of the angina producing also;

through obstruction to blood-flow, poorly nourished, weakened or fibrous myocardium. Or the sclerotic or atheromatous process may be quite limited, involving only the first portions of the aorta, but encroaching on the coronary arteries. Particularly in syphilis are the changes thus localized to the beginning of the aorta. In these cases the peripheral vessels may be normal.

Even with markedly sclerotic coronary, the peripheral vessels, and aorta as well, may show little or no change from the normal. Such a heart I saw in a man of 60, dying in his first attack of angina, or, rather, in his second, which came on twelve hours after the first. The coronaries were stiff-walled from calcareous deposits, and his heart not large. One may rightly urge the presence of peripheral sclerosis, murmur over the aorta, and large heart as strongly suggesting coincident sclerosis of the coronary, but one cannot exclude such sclerosis in the vessels of the heart or pronounce a cardiac pain as non-anginal because the peripheral vessels are normal.

Not a few seem inclined to discredit the possibility of angina unless the blood-pressure is persistently high, or at least is high just preceding or during an attack. That there is often persistently high blood-pressure is true. It is often true that preceding an attack there may be a rise. In some instances one may predict an oncoming attack because of the rise in pressure. In a case which I was privileged to see, the physician had the opportunity of measuring the change in pressure in the fatal attack. He had just finished reading the pressure, 160 mm. Hg, when the pain occurred and the mercury rose to 190 mm., death occurring before a hypodermic could be administered.

But one must be prepared for normal or subnormal readings. In some of the most serious cases, in fact, there is low blood-pressure, indicating perhaps a weakened myocardium. In a man of 54, with no general arteriosclerosis, I have seen the rough-walled left coronary plugged in its anterior branch with a thrombus,

producing sudden excruciating precordial pain. For the fifty hours that the patient lived the heart tones were barely perceptible, and the peripheral pressure extremely low. But in cases in which there is no such acute and extensive myomalacia cordis as was present in this instance, the pressure may be low for a long time and the patient busy about his work, though interrupted at times by the attacks.

Most physicians regard the existence of an aortic valve lesion of a sclerotic character as tending to strengthen their belief in the organic origin of the painful attacks, that is, such a finding points toward a true angina, and away from a so-called pseudo-angina. The same is true if the arch of the aorta is dilated uniformly, or in circumscribed aneurismal manner. The sclerotic or atheromatous lesion of the aorta or the valves leads one to suspect a similar trouble in the coronaries, or perhaps only at their mouths. And those who, like Allbutt, see in the aortic ring the seat of anginal pains, naturally interpret evidence of anatomic change in this locality as proof of the organic origin of the attack. Much depends on one's conception of the cause and nature of this disease. Some, however, hold so rigidly to the theory of coronary origin that, if aortic regurgitation or aortic aneurism be made out, or if there be strong reason to suspect aortitis, they will not call the seizures anginal, though the pain and other phenomena may be classic in every respect. They speak of such seizures as merely "the pain due to aneurism, aortic regurgitation," etc., but not the pain of angina pectoris; that is, coronary disease. This view, while held by only a few, is too narrow.

NUMBER AND DURATION OF ATTACKS

Another fallacy is connected with the number of attacks. Not a few physicians have been heard to express the opinion in concrete cases that, because the attacks were frequently repeated, they could not be anginal for, they assert, an individual never has more than a few;

he succumbs if there are numerous recurrences. This is utterly wrong. Repeated attacks of severe type may occur during periods varying from many days to many months. And it is no uncommon experience to meet patients whose milder attacks—the angina minor of some—are repeated several times in a single day. Neusser mentions a woman with twenty attacks a day. In one patient seen many times I witnessed over a period of three years the sufferings of this disease, there being at times as many as six and eight paroxysms in a day.

The attack is usually brief, being over in a few seconds or a few minutes. But in other instances it is more prolonged. After the acme of pain has been reached, there is a moderation, but still a residual pain, a soreness of skin in the precordia, and a numbness or pain extending down the arms, especially the left, to the elbow or fingers. The patients may suffer, therefore, for many minutes, or the pain may last for hours. In the patient already referred to, the one who had coronary thrombosis, the agonizing substernal pain lasted three hours, though death did not follow until fifty hours. Morison describes a case of coronary thrombosis with anginal pain, lasting twenty-three hours. This patient had previously suffered from milder attacks of angina. Opinions might differ as to the propriety of speaking of this more chronic state as angina, though it has the characteristics of the acute paroxysm, only less in degree, and longer drawn out as to time.

Where the status anginosus exists, one attack is rapidly followed by another, even on the slightest provocation or after no appreciable cause; some pain and soreness persist between the attacks, so that the patient is in a state of continuous pain and suffering, with frequently recurring exacerbations.

EXCITING CAUSE

The exciting cause of the attack is usually exertion, especially rapid walking. Some strange anomalies are at times seen. Thus a man may have an attack that is

brought on by the mere effort of walking about the room, while he dresses, or simply by stooping to lace his shoes. After his breakfast he may be obliged to stop two or three times on his way to take his train; yet for the rest of the day he is free, even though he may walk a considerable distance and eat rather freely at luncheon and dinner. One of my patients, in a suburb, could ride a bicycle to the station with fewer seizures than if he walked, though the streets were level and when afoot he never hurried. Another patient, a woman, has for two or three years been unable to walk two blocks without pain, necessitating her stopping to rest or to take nitroglycerin. She can remain for days together free from pain if she sits or lies still. Charles Sumner had attacks that at times seemed to be brought on by some sudden move, as by turning in his revolving library chair. Yet at other times, as when speaking in the Senate, he could be on his feet for hours, with all the mental excitement, bodily activity and gesticulation of earnest debate, and still be free from pain. It is well known that a fit of anger, a breath of cold air, an overloaded stomach, may precipitate a seizure.

These irregularities are to be remembered, and they are here referred to, because the opinion is at times expressed that attacks come on only after exertion; and, on the other hand, that, if an individual with supposed angina is able to walk briskly without an attack, it is proof against the existence of angina. While exertion and the other causes mentioned are the common provocative ones, these causes may produce an attack at one time and not at another, and often no cause can be clearly assigned for the outbreak any more than for some epileptic seizures.

INFREQUENCY IN WOMEN

All agree that true angina is comparatively rare in women, some statistics showing less than 5 per cent. Heberden saw three women in one hundred patients with angina. Undue importance is sometimes attached to the

infrequency in women, and one may thus be influenced away from a correct diagnosis. The error is easily understood, too, when in an individual case there are evidences of a strong neurotic taint. The undue excitement, the tendency to introspection and to exaggeration of symptoms, the desire for attention and sympathy, perhaps even the pronounced hysterical manifestations, may easily mislead one to the diagnosis of a functional, neurotic or so-called false angina. No inviolable rule can be given for the sure differentiation, but a study of the cardiovascular condition, the age, the exciting cause, the radiation of pain, the behavior and attitude during rather than after the attack will all be of help. It is certainly a cause for regret and chagrin to diagnose pseudo-angina and in a week or two have the woman die in an attack. In the case of a woman seen by many different physicians, all agreed as to the existence of a cardiac valvular lesion, and all agreed as to the existence of a marked neurotic, even hysterical, element, aggravated by a free habitual use of morphin. There was, however, a wide divergence of opinion as to the organic basis of the anginal attacks, some regarding them as wholly of the false type. A rest-cure, with breaking off of the morphin habit and marked improvement in every respect, lent color to the theory of pseudo-angina, but the woman died suddenly some two or three years later, as in angina. One has to keep clearly in mind what has been often said, but what is easily forgotten, that the cardiopath is often a neuropath. The hysterical woman may have underlying the nervous manifestations a serious pain-causing disease.

PAIN, UNCONSCIOUSNESS, IMMOBILITY, ETC.

Certain facts concerning the pain itself are worth repeating, for it is easy to have a stereotyped picture in mind, while in reality there are not a few variations.

I have never seen a case that I recognized as angina sine dolore, but since its description by Gairdner, it has

been a recognized form, and one cannot question its existence. Not long ago I heard Dr. J. M. Patton describe his experience in being called to the home of a colleague whom he found lying on the couch. In answer to the question as to what was the matter, the reply of the patient was that he did not know, he had no pain, but an indescribable sensation in the cardiac region, and an appalling sense of the presence of death, and "I'm mighty glad to see you," he said. In a minute more he suddenly expired. There was no feeble, rapid, irregular pulse; no dyspnea; no cyanosis; no pain—apparently angina save the pain.

It is surely wrong to state dogmatically that pain, in order to be anginal, must be severe, excruciating, unbearable. There are milder degrees. What is called angina minor must be viewed as in its essence of the same nature as the angina major. In one sense its recognition may be of greater importance than that of the major type, for it may lead to appropriate advice that may prolong life in cases in which were the disease unrecognized, a faulty mode of life might lead to early death.

The most typical radiation of pain is to the left side of the neck and down the left arm. But one must be prepared for odd radiation. The radiation is often down the right arm. In one of Morison's patients the right arm radiation was associated with sclerosis of the right coronary only. The pain may run down both arms. It often goes down the ulnar side. It may stop at the elbow, the wrist, or run to the little finger. Pain may start in the fingers, run up the arm, and finally centralize at the heart, seemingly a centripetal rather than centrifugal course. Pain, numbness and tingling may be complained of in the intervals between the attacks, and may be regarded as rheumatic and articular in origin. Pain to the jaw, to the ear, to the back may be described. And particularly confusing are the cases in which such odd radiations as to the epigastric, lumbar, renal and testicular region are seen. Tenderness of the

skin, as described by Head, may at times be made out. One of my patients, a woman, often has most profuse salivation with the substernal pain, that radiates to the left shoulder and arm. MacKenzie mentions this same salivation in his experience.

Unconsciousness, though unusual, is yet seen at times. On two occasions I have known a sufferer from angina to become unconscious, once at the climax of a paroxysm. Osler and others mention the same occurrence.

Immobility is a characteristic feature. The patient is afraid to move for fear the pain will be aggravated. He sits or stands motionless, at times almost statue-like; he will not lie down. Yet there are exceptions to these rules. Charles Sumner often walked about his library during an attack. An old colored man whom I recently had under my care in the County Hospital usually lay down, on the sidewalk or porch, or wherever he was taken, until the attack was over. His sudden death, two weeks after describing to me and to the class in clinic the typical manifestations of the disease, and the finding of sclerosed aorta, aortic valves and coronaries, confirmed the diagnosis of angina. This is, I think, the only patient I have seen who by choice would lie prone during an anginal seizure, though I have several times seen patients in a half-sitting posture, or have had such position described to me as the one assumed. A woman of 45, who had definite loud basic murmur, apparently due to roughened aorta and aortic valves, would, during the pain of angina, get on her hands and knees in bed. She was neurotic and admitted that there was a hysterical element in her case, but insisted that the pain was real and that this position gave her the greatest relief.

Once or twice I have had the diagnosis of angina questioned because of the prominence of eructation or vomiting. Flatulence or vomiting may be marked. At times the attack ceases with the belching of gas or the raising of the contents of the stomach. That a stomach

distended with gas or food may cause epigastric or precordial distress is a well-known fact, but it should also be remembered that true angina not infrequently follows a hearty meal, or is accompanied by striking gastric symptoms.

PROGNOSIS

A word about prognosis. There is in some quarters the opinion that the disease is not only inevitably fatal, but that death is sure to follow in a short time, or after two or three attacks. There is surely good reason for viewing this condition as one of extreme gravity. Death, and often sudden death, is the common result. But it is also worth noting that the fatal termination may be deferred for years and, exceptionally, complete recovery seems to ensue. If one includes under the head of angina pectoris the toxic, as for example, tobacco anginas, and the neuroses with precordial angina-like pains—the so-called pseudo-anginas—the mortality percentage, while high, would not be so startlingly large. But even excluding the neurotic forms and limiting the statement to the true cardiovascular types, the mortality is not 100 per cent., as some think; and even in the fatal cases death may be postponed for many years. In a paper recently presented to the Chicago Medical Society, Dr. Forchheimer of Cincinnati cited one of his cases, in which the first attack had been seventeen years before death. Dr. Billings had seen a patient live fifteen years after the first paroxysm. A physician whom I cared for had his first severe and nearly fatal angina seven years before his fatal attack. Morison describes a case in which the pains recurred at intervals for seven years. Stokes had a case in which for ten years the patient suffered from attacks of excruciating severity. John Hunter had attacks for twenty years.

The recognition of the malady, the regulation of the mode of life to that most suited to the cardiovascular condition, involving, as it often does, change in diet and

habits of work, the proper use of remedial drugs; in a word, appropriate treatment may materially alter the prognosis. The condition of the heart and vessels as to aneurism, valvular disease, general sclerosis, myocarditis and fatty changes, must determine to a marked degree the length of life. And so, too, does the condition of the kidneys.

NITRITES AND DIGITALIS

I wish to refer briefly to certain fallacies concerning the use of nitrites and digitalis.

The nitrites have, especially of late, been held by some in less repute than formerly, because they fail completely in some instances to relieve or ward off the attacks. Others seem so convinced of their efficacy that, when in a case of supposed angina the nitrites fail to relieve the suffering, and to relieve it promptly, they conclude that they are dealing with something different from true angina. Now, the truth seems to be that nitrites in some cases give most prompt, marvelously prompt relief. The testimony of many physicians is available on this point. It is hard to understand, then, how some good men—Romberg, for example—regard this remedy as either of no benefit or of very insignificant value, at least during a seizure. Unless convinced by repeated trials as to its uselessness in the attacks, no patient should fail to keep in his pocket either the pearls of nitrite of amyl or the pill or tablet of nitroglycerin, gr. 1/100 to 1/50. Some attacks are surely cut short by the use of these remedies, and often the patient has a slight warning of the onset, and the timely use of the drug may prevent a paroxysm.

No matter how strong the prejudice against the use of digitalis in cardiac hypertrophy and general arteriosclerosis may be; no matter what may have been said against its employment in weakened myocardial states, there can be no question that in some cases of angina—not easily described, either—this drug does more good than all the iodids or nitrites.

SUMMARY

These views may be summarized by making the statements as a series of negations:

1. With "true," organic cardiovascular angina pectoris there cannot always be made out peripheral arteriosclerosis, cardiac hypertrophy and high blood-pressure.

2. The finding of aneurism or lesion of the aortic valves does not exclude angina, but rather argues in its favor.

3. The attacks are not always few in number and brief in duration; they do not occur solely after exertion.

4. While the prognosis is grave, life is not necessarily limited to a few months.

5. The disease is by no means to be excluded because the symptoms are found in a woman, even in a nervous or hysterical woman.

6. The pain is not necessarily severe; it may be mild or even lacking; its radiation is variable.

7. The statement that the patient is always conscious, that he is always immobile and erect must be modified so as to read "usually" instead of "always."

8. Eructations or vomiting during an attack do not argue conclusively against the cardiovascular origin of the angina.

9. It is not correct to look on the nitrites as of no benefit in relieving symptoms; nor, on the contrary, is one justified in concluding that a case unrelieved by nitrites is not angina.

10. Digitalis is not necessarily contra-indicated; it is often of very great value.

Closer observation of the atypical as well as the typical cases, with collocation of the results with those of anatomic and experimental studies will lead to unifying knowledge concerning the pathogenesis of this disease, to greater precision in its recognition, and to more appropriate treatment.

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ABSTRACT OF DISCUSSION

DR. JOSEPH L. MILLER, Chicago: If we followed the statements made in text-books regarding angina pectoris, the diagnosis of this disease would frequently not be made. A statement often made is that patients suffering from angina pectoris always remain quiet, whereas, many patients with typical attacks of this disease will move about. I believe that the term "pseudo-angina" should be entirely abandoned. Patients with symptoms resembling angina pectoris, in whom we can exclude an ordinary neuritis, should be considered as suffering from true angina. I do not believe that the value of digitalis in angina pectoris is fully appreciated; I think that there are many patients who receive permanent benefit when taking this drug, the attacks recurring less frequently. It has been shown experimentally that a much more extended ligation of the coronary artery may be made without serious consequences when the animal is under the influence of digitalis or strophanthus, and I think that the same holds true in human beings. There may be obstruction of a coronary artery with less serious consequences if the heart is under the influence of digitalis.

DR. GEORGE W. MCCASKEY, Fort Wayne, Ind.: I had under observation last year a patient who had anginous attacks occurring sometimes during exercise, but the majority occurred during the night. The patient awakened in the night with this precordial pain and a sense of approaching death, etc. These attacks were as typical during the night as during the day. This patient referred to finally died and came to autopsy. The heart was exhibited to the Fort Wayne Medical Society, and showed both coronary arteries extensively involved. There is a group of cases which has interested and troubled me very much, in which this precordial pain is more or less persistent, with occasional severe exacerbations. Whether such cases should be placed in the group of angina pectoris is a question that must be answered according to the definition of angina pectoris. But there are some cases, indistinguishable by their symptoms, in which there is serious organic disease and in which the heart is able to adjust itself to the new conditions. If the nutrition be improved, some of these patients will make a relative recovery.

I recall the case of a patient, aged 60, who came to me about four years ago, suffering from severe typical attacks of angina pectoris. His family physician, on several occasions when called in to attend him, thought he would die. I placed him on the usual treatment. He was given the nitrites, small doses of digitalis, and iodids. This patient made a complete symptomatic recovery. I saw him within the last six months and he apparently is in good health.

Another patient that I now have under observation has more or less persistent pain. This man is very intelligent and co-

operates with me in observation of his case. He says that he never was free from a sense of constriction, but what annoys him most is this pain, which at times is almost continuous; at other times he has a sense of pressure. If he exercises he brings on an attack. He has no paroxysms during the night. Still another case of an entirely different type was in a boy of 11, who, about 3 years ago, had what apparently were typical attacks of angina pectoris. The precordial pain lasted a few minutes and the attacks occurred mostly during the night, though they also occurred at times after exercise. One would not expect any trouble with the coronary arteries in a boy of this age; he made a complete recovery and is well to-day.

I think that the majority of these cases occur about middle life or later, and are due to changes in the coronary arteries. But what causes the pain in angina pectoris? I think there must be some interference with the circulation in the heart muscle or disturbance of the neuromuscular mechanism of the heart. This is certainly far from a satisfactory explanation, but is the best we have at present.

Dr. Gustav Baar, Portland, Ore.: Some years ago, Billroth said that in cases of angina pectoris he gave one-half grain of digitalis leaves every day and that the patients could then keep at work. Since then, I have employed this agent in this form and dosage, and with very good results. At the same time I must caution against the promiscuous use of digitalis in heart disease. I have seen a number of "bronchial asthma" patients in collapse—cold extremities, imperceptible pulse, etc. In these cases I have injected 1 mg. of strophanthin, intravenously. A young woman, after injection of this amount of strophanthin, within three minutes displayed bounding and rapid pulse and is alive to-day. Through my experience in this case I was much encouraged in the use of strophanthin. Some time later, I was called to see a patient with "angina pectoris," who had been under the digitalis treatment for three years. I found this patient in collapse and injected 1 mg. of strophanthin; after injecting the drug I left, but was called back at the street corner: the woman was dead. Undoubtedly, the death was due not to the angina pectoris, but to the strophanthin. Since then, I have given up the use of strophanthin in any case of arteriosclerosis, a condition which is usually associated with angina pectoris.

Dr. Scott P. Child, Kansas City, Mo.: I should like to report a case of angina pectoris in support of Dr. Herrick's contention that many cases are atypical. The patient was an active Episcopal bishop of western Missouri, aged 70, height 6 feet 2 inches, weight 180 pounds. While attending to the duties of his diocese, and following an evening meal, he ran upstairs and was immediately taken with what he termed

the most severe pain he ever suffered. The pain, beginning at the base of the heart, back of the sternum, ran up into the neck and jaws of both sides and down both arms to the finger tips. The pain lasted an hour and a half, being relieved only by a hypodermic injection of morphin. During the attack of pain the patient suffered from intense cold, which was followed by profuse perspiration. Two days following the attack, the pulse was quite regular, the rate varying from 120 to 130; the blood-pressure in the right arm was 140 mm. Hg, that of the left 126 mm. Hg. This patient has been under my observation for two years (no previous attack suffered), with a well-established myocardial insufficiency, the heart being enlarged well beyond the nipple line and down to the sixth interspace. So far, no valvular signs have developed. This patient for several years has had evidence of interstitial nephritis, with a constant albuminuria, hyaline, and frequently granular casts. Two days following this attack of angina, the urine revealed 0.5 per cent. of albumin and numerous hyaline and granular casts. At the end of a week, with rest in bed and a regulated diet, the pulse was down to 92 and regular, the blood-pressure was low, and the urinary findings very much improved.

Dr. John A. Witherspoon, Nashville, Tenn.: It is unfortunate that so many physicians are looking for such cases of angina pectoris; they look for cases of such severity that the patients are made perfectly quiescent, with fixation of the body, cyanosis, and so forth. They do not seem to realize that there may be cases of angina pectoris, with intermittent attacks of mild character, which have been threatening the patients for years. I learned long ago that the pulse in angina pectoris was unreliable; I have found a low pulse and a rapid pulse in bad cases, as well as in mild cases of this disease. If these cases are properly conducted and properly managed between the attacks the attacks will become less severe. Like Dr. McCaskey, I like to give the iodids with the digitalis.

I doubt very much the diagnosis of angina pectoris made in the case of the boy of 11 years; I have yet to see a true case of angina pectoris occurring in a patient so young. We are likely to get an increase in the blood-pressure, with evidences of an accentuated second sound of the heart, but no evidence of atheroma of the coronary arteries. Many of these cases may be explained and will be found not to be due to angina pectoris. The nitrites act happily in some cases, but when most needed they most often fail to give relief. It is especially in the bad cases that the nitrites seem to fail us.

Dr. Allen A. Jones, Buffalo: We cannot always judge of the condition of the coronary circulation in the heart from the condition of the peripheral circulation as we see and feel it. I have now under observation a patient with typical

attacks of angina pectoris. He has suffered any number of attacks; he is an individual in middle life, and pulse, blood-pressure, and heart are practically normal. The pain may be present in an unusual situation, and not in the classical situation, precordial and running to the left shoulder and left arm, or to the wrist and thumb. In a paper read at a session of this Association in Atlantic City some years ago, I called attention, in discussing "Abdominal Symptoms of Thoracic Disease," to the fact that we might encounter epigastric pain as well as cardiac. The pain may be typically epigastric, and may be called gastralgia; in fact it often is. Between the attacks of angina pectoris it is not an uncommon experience to find individuals complain bitterly of gastric symptoms, and more especially of a collection of gas in the stomach, a "pneumaptosis," the pressure of which on the diaphragm frequently leads to an attack. I think that one should exercise great caution in his choice of cases; in a patient with high blood-pressure, with cardiac hypertrophy and with a competent heart, digitalis is not to be used except under extreme watchfulness. On the other hand, given a case of angina pectoris with opposite conditions, in a frail and spare individual with low blood-pressure, and with attacks often coming on after exercising, then the administration of small doses of digitalis over a long period frequently does good.

Dr. James B. Herrick, Chicago: The question of treatment I purposely omitted from my paper, except the few words concerning digitalis and the nitrites. I agree, however, with what has been said in regard to the use of the iodids; they certainly are of great benefit.

THE RELATION OF BLOOD PLATELETS TO HEMORRHAGIC DISEASE

DESCRIPTION OF A METHOD FOR DETERMINING THE BLEEDING TIME AND COAGULATION TIME AND REPORT OF THREE CASES OF HEMORRHAGIC DISEASE RELIEVED BY TRANSFUSION

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It is my purpose in this paper to report three cases and experiments which furnish additional evidence to show that the blood platelets play a part in stopping hemorrhage, and that one type of hemorrhagic disease may be attributed to an extreme reduction in the number of platelets. The cases possibly explain the relief which sometimes follows transfusion in hemorrhagic disease. It is my purpose also to describe a method for studying hemorrhage called the bleeding time, and to describe briefly a simple method for determining the coagulation time.

In the cases there was marked hemorrhagic diathesis, a normal coagulation time, and almost an absence of platelets. Transfusion was performed in each case. After transfusion there was a marked increase in the number of platelets and remarkable relief of hemorrhage. When the platelet counts returned to their previous low level, hemorrhages returned. Later in the course of the disease in two of the cases, the platelet count rose spontaneously and this rise also was followed by relief of hemorrhage. The cases are reported to show the marked

dependence of pathologic hemorrhage in this type of disease on the reduced numbers of platelets. The experiments are reported briefly to show that platelet counts reduced experimentally by benzol are not associated with changes in the coagulability of the blood which account for the hemorrhages of the condition and suggest that this type of hemorrhagic diathesis is due directly to the lack of platelets.

A METHOD FOR DETERMINING THE BLEEDING TIME

A small cut is made in the lobe of the ear. At half-minute intervals the blood is blotted up on absorbent paper. This gives a series of blots of gradually decreasing size. Each blot represents one-half minute's outflow of blood. The rate of decrease in the size of the blots shows the rate of decrease of the hemorrhage. The cut should be made of such a size that the first half minute's outflow of blood makes a blot 1 or 2 cm. in diameter. The total duration of such a hemorrhage is called the bleeding time.

Figure 1 (A, B, C) was made from cuts of different size. These sets of blots show that within certain limits the duration of a hemorrhage does not depend on the size of the cut. If these figures represent capillary hemorrhages it is evident that a large number of capillaries will stop bleeding as rapidly as a small number.

The normal bleeding time varies from one to three minutes.

The bleeding time is slightly delayed (five to ten minutes) in severe anemia (Fig. 2).

Great delays in the bleeding time were found in, (1) cases in which the platelet count was excessively reduced (ten to ninety minutes—Fig. 3), (2) cases in which the fibrinogen content of the blood was excessively reduced (ten minutes to twelve hours), and (3) experimental animals in which both platelets and fibrinogen were reduced.

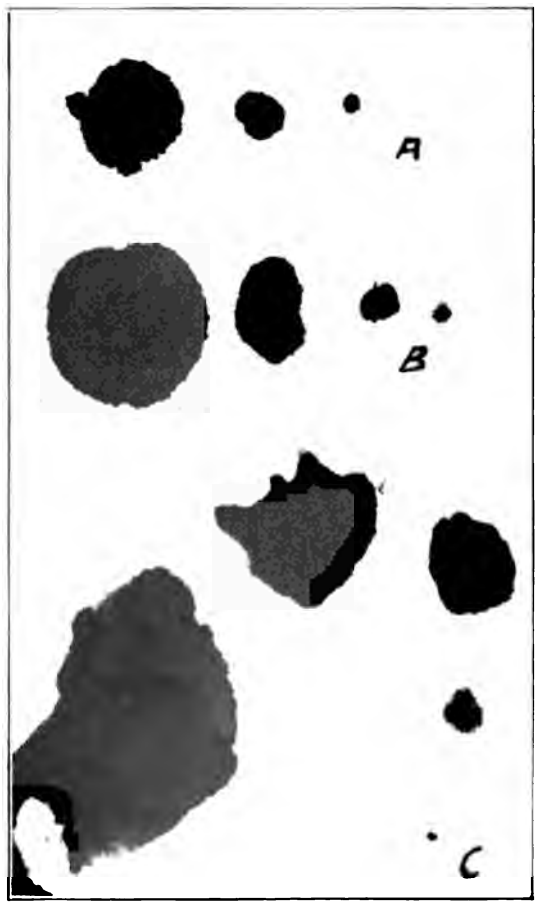

Fig. 1.—Normal bleeding times; A, from small cut; B, from larger cut; C, from very large cut.

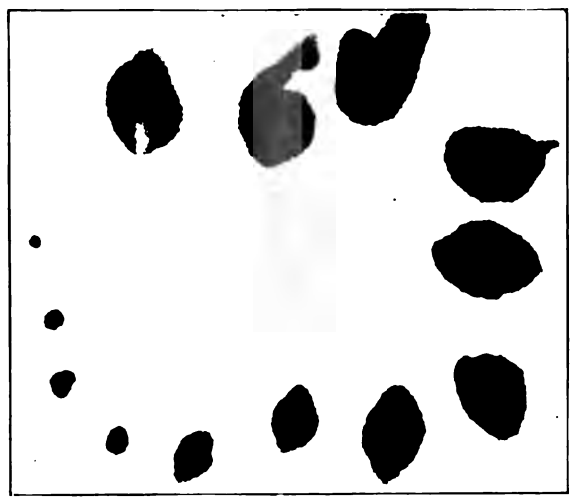

Fig. 2.—Slightly delayed bleeding time. From a case of secondary anemia.

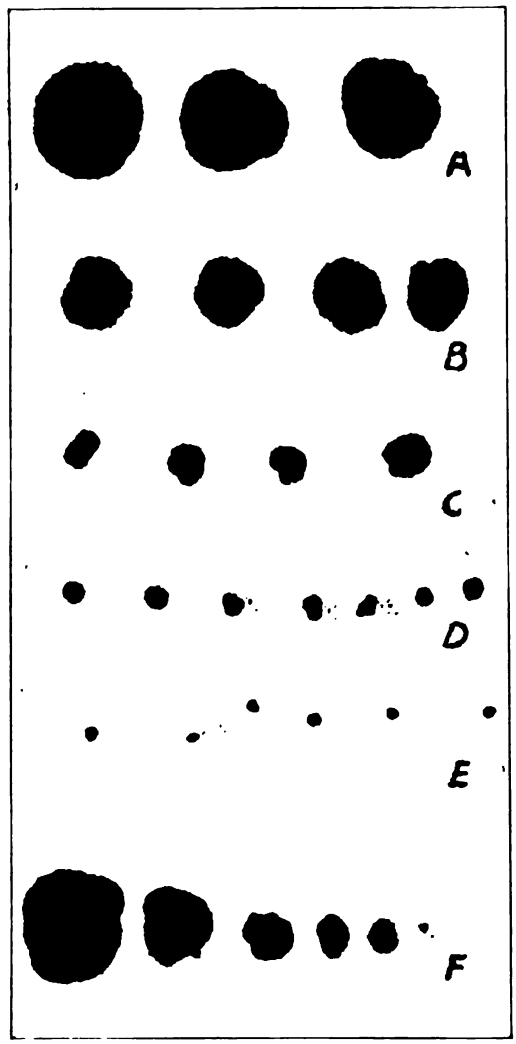

Fig. 3.—Great delay in bleeding time. From Case 1. Platelet count 3,000, coagulation time normal. The blots in Series A were taken immediately after the ear was pricked; Series B, 20 minutes; C, 40 minutes; D, 60 minutes, and E, 80 minutes later. The bleeding time at this time was 90 minutes. Series F, showing a normal bleeding time, was taken after the transfusion. Platelet count was then 110,000.

It is remarkable that the bleeding time is independent of the coagulation time. The bleeding time was normal in several cases of jaundice in which the coagulation time was very much delayed. Two of these patients died of pathologic hemorrhage. It was also normal in a patient with hemophilia, who had a slight delay in the coagulation time and pathologic hemorrhage. The bleeding time was found to be normal in several types of purpura hemorrhagica in which the platelet counts were normal. It is difficult to explain why these patients had hemorrhage into the tissues, from mucous membranes, and from operation wounds, and at the same time had normal bleeding from ear-pricks.

The bleeding time, then, in types of disease associated with low platelet counts, or with a reduced quantity of fibrinogen shows a tendency to prolonged hemorrhage. In these types of disease, a delayed bleeding time is a more reliable indication of hemorrhagic diathesis than hemorrhagic symptoms, for such symptoms usually depend on general and local causes. The latter are, of course, not constant. In the cases reported in this paper the bleeding time was invariably delayed when pathologic hemorrhage was evident, and was often considerably delayed before hemorrhage began.

The method is apparently of no value in determining the tendency to bleed in jaundice and hemophilia, and in the types of purpura hemorrhagica which have normal platelet counts.

A SIMPLE METHOD FOR DETERMINING THE COAGULATION TIME [1]

The apparatus consists of a slide on which are mounted two 5 mm. disks. One disk is covered with the blood to be tested. The other is covered with normal blood. The

1. This method is a modification of Hinman and Sladen's slide method (Johns Hopkins Hosp. Bull., 1907, xviii, 207). The principle was first used by Milian.

two drops of blood should be of about the same depth. The slide is then inverted over a glass nearly full of water kept at 40 C. and is covered with a warm, damp cloth. The coagulation time is determined by holding the slide in a vertical position for a moment. When the end point is reached the drop does not hang, as in Figure 4 *a*, but retains the contour of a perfect sphere (Fig. 4 *b*). The end point appears sharply and is easily determined.

The normal coagulation time by this method varies from five to seven minutes. A very shallow drop clots

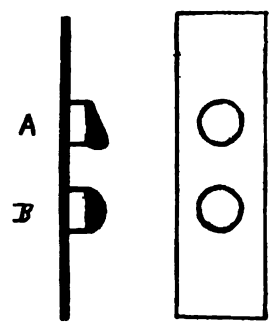

Fig. 4.—Instrument for determining the coagulation time.

one to two minutes sooner than a very deep one. The normal blood can be used for a control, or can be used for obtaining a comparative time.

If simply the comparative time is desired, the temperature of the water may be allowed to vary between 35 and 40 C., and the glass may be covered with the hand instead of a damp cloth. A delay of two minutes can be easily determined by this method.

PLATELET COUNTS

Wright's method[2] was used in making the platelet counts. According to this method the blood is drawn up in a 1-100 pipette, mixed with a solution of cresyl blue and potassium cyanid and counted by the red cell

2. Wright and Kinnicutt: Tr. Assn. Am. Phys., May, 1910.

technic. The red cells are laked by this solution and the leukocytes and platelets are stained. This is a great advantage, for the platelets can be easily recognized and can be counted with a high dry lens. The counts made by this method are uniformly lower than those made by Pratt's method.[3] This method, however, gives constant results if care is used in the technic. The normal count, according to Wright and Kinnicutt, varies from 225,000 to 325,000.

REPORTS OF CASES [4]

CASE 1.—*Summary.*—Acute purpura hemorrhagica. Purpura; spontaneous hemorrhages; practical absence of platelets; delayed bleeding time; normal coagulation time. This case is of interest in showing relief of hemorrhage, both after the rise in the platelet count following transfusion, and after a spontaneous rise in the count which occurred later in the disease.

History.—S. M., a man aged 20, Armenian, tailor, was admitted to Massachusetts General Hospital May 8, 1909, complaining of epistaxis. The family history is negative for hemorrhagic disease. The patient has always been strong and well, and has had no serious illnesses. He has never had prolonged epistaxis, spontaneous ecchymoses, joint trouble, urticaria, nor abdominal crises. His digestion has always been good. For three weeks before admission to the hospital he had been feeling run down, and had had slight sore throat. For five days he had been troubled with persistent epistaxis. He noticed that his urine was high-colored, his stools black, and that he was covered with purpuric rash. There was nothing further of importance in the history.

Examination.—The patient was a well-developed and well-nourished young man, pale and weakened by loss of blood. A small amount of blood was then oozing from the border of his gums, and nasal mucous membranes. Scattered over his entire body, including the soles of his feet, mucous membranes, tongue, and scleræ, were fine muscular purpuric blotches, 1 to 5 mm. in diameter. In places, especially on the lower extremities, they were confluent, and covered areas 2 to 3 cm. in

3. Pratt, J. H.: A Critical Study of the Various Methods Employed for Enumerating Blood Platelets, THE JOURNAL A. M. A., Dec. 30, 1905, p. 1999.

4. I wish to express my thanks to Dr. F. T. Murphy, Dr. Hugh Cabot, Dr. L. A. Conner and Dr. R. D. McClure for permission to report these cases, and to Dr. J. H. Wright for his kind assistance in making the platelet counts.

TABLE 1.—CASES OF HEMORRHAGIC DISEASE IN WHICH THE PLATELET COUNT, COAGULATION TIME AND BLEEDING TIME WERE DETERMINED

Disease.	No. of Cases.	Symptoms.	Plate Count.	Coag. Time.	Fibrinogen Content of Blood.	Bleeding Time.	Other Diseases which may Give Similar Blood and Similar Symptoms.
Idiopathic purpura hemorrhagica.	3	Purpura, spontaneous hemorrhages.	Below 20,000...	Normal...	.....	60 min.+	Pernicious anemia, lymphocytic leukemia, nephritis, typhoid fever.
Aplastic anemia.....	2	Ecchymoses, epistaxis.....	Low.....	Normal...	Nor. in experimental aplastic anemia.	Delayed.	
Chronic Ulcerative colitis.	1	Melena.....	20,000 to 30,000	Normal...	.....	10-20 min.	
Chloroform poisoning.....	Dogs. 3	Bleeding from gums and operation wounds.	Normal or slightly reduced.	Normal...	Excessively reduced.	Hours....	Phosphorus poisoning, hemorrhagic smallpox.
Jaundice..	2	Hemorrhage after operation.	Adundant in smears.	30 min.... 40 min....	.....	1-2 min....	
	1	Purpura hemorrhagica....	350,000.....	8 min.....	Probably normal in jaundice.	3 min.....	
	8	No symptoms.....	Abundant in smears.	Nor. or delayed.	.....	1-3 min...	
Hemophilia.....	1	Bleeding from wound; hematoma in knee.	350,000.....	9 min.....	Normal in hemophilia.	2 min.....	
Purpura simplex.....	2	Purpura.....	Abundant in smears.	Normal...	.....	Normal...	
Henoch's purpura.....	1	Purpura, intestinal crisis, melena.	275,000.....	Normal...	.....	Normal...	
	1	Purpura, urticaria, angioneurotic edema.	300,000.....	Normal...	.....	Normal...	
Nephritis.	4	Epistaxis.....	Abundant in smears.	Normal...	.....	Normal...	
	1	Ecchymoses					

TABLE 2.—DETAILED FINDINGS IN CASE 1

Date.	Platelet Counts.	Plates in Stained Blood Smears.	Bleeding Time. (Minutes.)	Coagulation Time.	Urine.	Stools.	Epistaxis.
May 8	6,000	1-2 per smear	47	5 minutes	Smoky	Tarry	Moderate.
May 9	None seen	None seen	90	5 minutes	Smoky	Tarry	Moderate.
May 10	3,000			5 minutes	Smoky	Tarry	Moderate.
May 11		2 per smear	50 +	4½-5 minutes	Smoky	Tarry	Extreme.
(Transfusions).							
May 12	123,000	1-3 in each field.	3	4½ minutes	Clear	Tarry	None.
May 13		1 in 3-4 fields	3			Yellow	None.
May 14			30		Clear		None.
May 15		3 per smear	40		Clear	Occult blood.	Slight.
May 16		1 per smear	50	5 minutes			Moderate.
May 17	1,500	3 per smear	50		Clear	Fresh blood.	Moderate.
(Spontaneous increase in the number of platelets).							
May 18						Occult blood.	None.
May 19		1-6 per field	2				None.
May 23			2	5 minutes	Clear	No blood	None.
May 24	84,000	3-8 per field	4				None.

BLOOD EXAMINATION

May 8, R. C., 3,264,000; Hbg., 50%; W. C., 5,000
May 10, R. C., 3,260,000; Hbg., 50%.
May 11, R. C., 2,700,000; Hbg., 40%; W. C., 7,000
May 12, R. C., 3,600,000; Hbg., 46%
May 14, R. C., 3,500,000; Hbg.
May 16, R. C., 3,444,000; Hbg., 55%; W. C., 6,000
May 24, R. C., 5,000,000; Hbg., 70%; W. C., 2,400

diameter. Retinæ were free from hemorrhage. There were a few mucous râles at the lung apices, and a soft systolic blow at the base of the heart. The spleen edge was palpable just below the costal margin. There were no telangiectases on his skin or mucous membranes. Blood-smears showed almost a total absence of blood-plates, 6,000 by count. On the following day the counts were even lower. The bleeding time was forty minutes. The coagulation time was normal.

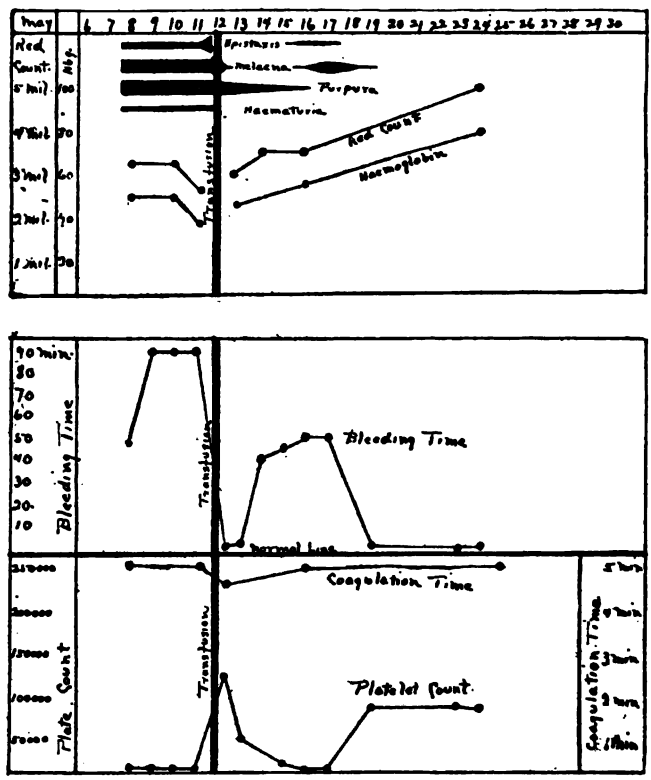

Fig. 5.—Chart of Case 1.

The course of disease can be followed by the chart (Fig. 5). During the first four days in the hospital there was an almost constant oozing of blood from the nose, which could be controlled for only short periods of time by packing. The stools and urine each day contained considerable blood.

Transfusion.—On May 11, the patient lost over a pint of blood from the nose, and his condition became so critical that

he was transfused at 2 a. m. by Dr. F. T. Murphy. An Armenian friend of about the same age was donor. That a large amount of blood was given by transfusion was evident from the improvement in the patient's general condition, color, and pulse, and from the rise in the pulse-rate of the donor.

Course of Disease.—The platelet count, taken six hours after transfusion, was 123,000. The bleeding time had dropped to three minutes. The coagulation time was practically unchanged. Epistaxis had stopped before this time, and the packing had been removed from the nose. The urine was then free from blood. The stools on the following morning were light yellow, but contained a small amount of occult blood. No fresh purpuric spots appeared and the ones present began to fade, disappearing completely in five days. Thirty-six hours after transfusion it could be seen from stained smears that the platelets were decreasing rapidly in number, and on the third day one could be found only after prolonged search. At this time the bleeding time was again delayed. The day following this the patient's nose began to bleed and fresh blood appeared in the stools. Since the onset of the disease the patient had had an irregular temperature, varying from 99 to 103 F. This came to normal, except for slight remissions, on May 20. Apparently the disease had run its course, for at this time plates reappeared in the blood (80,000), and hemorrhage from ear-pricks would last for only three minutes. There was no further epistaxis or melena. Convalescence was uneventful, and since then the patient has continued his vocation without symptoms.

Differential Counts.—Made on May 8, 9, 12, 15, 23. Polymorphonuclear neutrophils made up from 80 to 86 per cent. of the cells. The remainder were lymphocytes with an occasional mast-cell and eosinophil. Only one blast was seen.

Red Cells.—Moderate variation in size. Shape normal. Moderate amount of achroma and polychromatophilia. An occasional stippled cell.

Coagulation Time.—The comparative method was used. The temperature was kept constant at 40 C. My blood, which had a coagulation time of five to six minutes, was used as a control. Usually several determinations were made and the average taken.

Platelet Counts.—Pratt's method was used in making the platelet counts on May 8, 9 and 10. The other determinations were made by Wright's method. The variations in the platelet count were so marked that estimations from stained cover-glass preparations of the blood proved satisfactory. Smears were looked over carefully with oil immersion lens on the days mentioned, and the number seen per smear or field averaged.

Retraction of Clot.—The clot was non-retractile after standing forty-eight hours on May 11 and 16. It retracted normally on May 12 and May 23.

Bleeding Time.—Determined by the method described. As a rule several determinations were made and the times averaged.

Urine.—Normal except that it contained a sediment of red cells and a slight trace of albumin on May 8 to 11. It contained no sugar, bile, peptone, albuminose, or nucleoproteid.

Stools.—May 8 to 12, rather copious, soft and black; from May 13 to 16, soft and light yellow (milk diet). Guaiac test was faintly positive on May 13 and 14; strong on May 15. On May 17, the stools were brown and soft and mixed with about 50 c.c. of fresh blood and a little mucus. On May 18, the stools gave the guaiac test. May 19 to 23, the guaiac test was negative. No parasites or ova were found.

The patient was seen eleven months after his illness and was then apparently strong and healthy. White count 4,700. Polymorphonuclears, 66 per cent.; lymphocytes, 34 per cent.; hemoglobin, 85 per cent. Plates 240,000. Bleeding time one minute.

CASE 2.—*Summary.*—Chronic ulcerative colitis; melena; reduced platelet count; delayed bleeding time; normal coagulation time. The bleeding time was normal after the rise in the platelet count following transfusion. The melena was slightly increased by transfusion. The case is of interest in showing a difference between the curative influence of transfusion in normal and in pathologic hemorrhage. Although the general tendency to hemorrhage (shown by the shortened bleeding time) was markedly diminished by transfusion, hemorrhage from the intestinal ulcers was increased. The case shows the difficulty of judging the tendency to abnormal hemorrhage by hemorrhagic symptoms alone.

History.—A. C., American, a boy aged 8, was admitted to Massachusetts General Hospital Nov. 15, 1909, complaining of weakness and diarrhea. The family history is negative for hemorrhagic disease. The patient's early life was normal. He had had no serious acute illnesses. After the age of 2 he suffered almost continually from diarrhea. He developed slowly, was always thin, and never strong enough to go to school. After the age of 4, there were four periods of a month or less in which the stools contained considerable blood, and the patient became pale and weak. He bled excessively from a trivial cut once. He never had ecchymosis on slight injury, joint disturbance, nor other evidence of hemorrhagic disease. For a month before admission to the hospital, the diarrhea was more severe, the stools contained blood, and the boy was becoming pale and weak.

Examination.—The patient was poorly developed, thin and pale, skin clear. Except for evidence of anemia, there was

nothing of interest on physical examination. There were no telangiectases on the skin or mucous membranes, and no jaundice. Blood-smears showed a scarcity of the plates. Counts varied from 20,000 to 30,000. The bleeding time was twenty minutes. The coagulation time was normal.

During the first two and one-half weeks in the hospital a prominent symptom was diarrhea. The patient had from eight

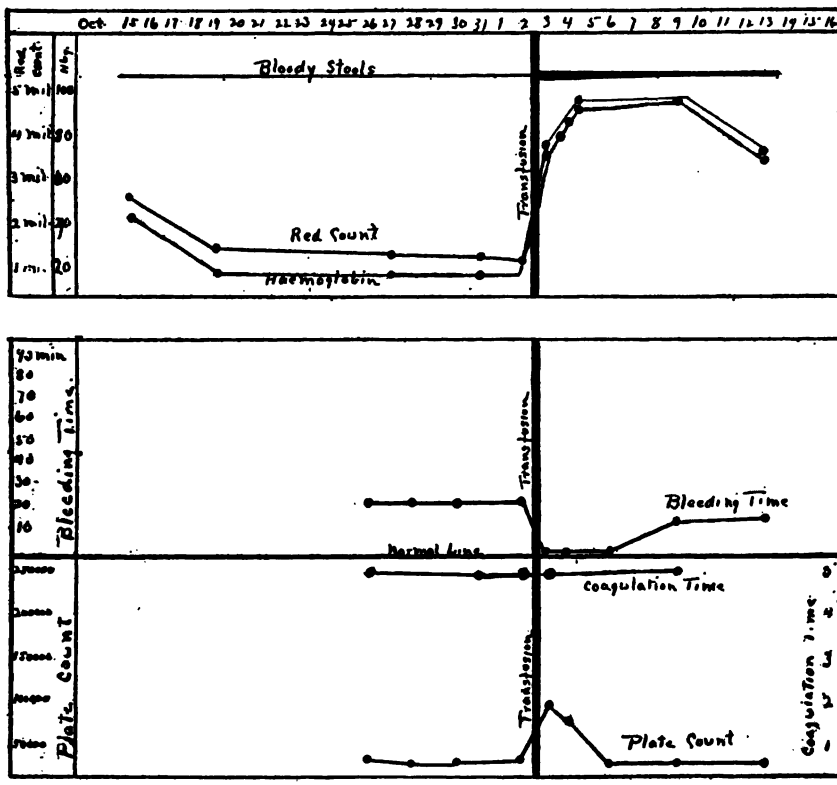

Fig. 6.—Chart of Case 2.

to thirty stools a day, which consisted mostly of thin pus, and often contained a small amount of blood and mucus. The patient's temperature varied from 98 to 103 F.

Transfusion.—On November 3 the patient was transfused by Dr. Hugh Cabot, preparatory to cecostomy. The child's father was donor. Following transfusion there was improvement in general condition and color. The temperature came to normal, and the pulse-rate dropped from 150 to 110.

Course of Disease.—The platelet count, taken two hours after transfusion, was 90,000, and the bleeding time was two minutes. The coagulation time was unchanged. The amount of blood in the stools, however, was increased. In interpreting this result it must be borne in mind that the patient had an extensive chronic ulcerative colitis (proved by autopsy), a condition which may cause melena when the blood is normal. The increase following transfusion was thought to be due to overfilling of the blood-vessels. Cecostomy was performed on the following day without excessive hemorrhage. As in the previous case, the platelets introduced by transfusion disappeared rapidly, and in a few days the count reached its former low level. The bleeding time again became delayed. The melena continued. The boy gradually became anemic, febrile, and died about a month later of septicemia.

Autopsy.—Chronic ulcerative colitis and enteritis. Extensive inflammatory thickening of the intestinal walls. Chronic pleuritis. Hyperplasia of mesenteric lymph-nodes. Streptococcus obtained from heart blood.

DETAILED FINDINGS IN CASE 2

Date.	Platelet count.	Bleeding time (min.).	Coagulation time.
10/26	32,000	20	Normal
10/28	23,000	20	.....
10/30	22,000	20	Normal
11/ 2 ..... (Transfusion).	20,000	20	5 min.
11/ 3	89,000	3	5 min.
11/ 4	72,000	2½	.....
11/ 6	25,000	3	Normal
11/ 8	.....	..	.....
11/ 9	25,000	10	.....
11/13	.....	10	.....

BLOOD EXAMINATION

10/15,	R. C.....3,600,000	Hbg., 42%	White Counts, 3,700
10/19,	R. C.....1,600,000	Hbg., 20%	White Counts, 3,100
10/31,	R. C.....1,224,000	Hbg., 15%	White Counts, 4,700
11/ 2,	R. C.....1,200,000	Hbg., ...	White Counts, ...
11/ 3,	morning.....3,280,000	Hbg., 70%	White Counts, 3,800
11/ 3,	afternoon ...3,416,000	Hbg., ...	White Counts, 2,200
11/ 4,	.....	Hbg., 85%	
11/ 9,	.....	Hbg., 90%	
11/13,	3,600,000	Hbg., 70%	

Differential Counts.—Polymorphonuclear neutrophils varied from 40 per cent. to 60 per cent. The remainder were lymphocytes with an occasional mast-cell and eosinophil. No blasts seen.

Red Cells.—Moderate variation in size. Shape normal. Moderate amount of achroma and polychromatophilia. No stippling.

Coagulation and Bleeding Time.—Determined as in Case 1. The platelets were counted by Wright's method.

Retraction of Clot.—On October 26 there was a very slight retraction of the clot after twenty-four hours; on November 3 and 4 a moderate amount of retraction; on November 9 no retraction.

Urine.—Normal.

Stools.—Eight to thirty a day, throughout the patient's illness. Small in amount and of pea-soup consistency. Stools contained considerable pus, a small amount of food residue and mucus. During the first few days, after admission, they contained considerable fresh blood. For ten days before transfusion they contained very little blood. After transfusion the stools were port-wine in color and contained considerable blood. Melena continued until death. Stools contained no parasites or ova. Cultures taken frequently showed only the colon bacillus.

CASE 3.—*Summary.*—Chronic purpura hemorrhagica[5]: Ecchymoses; purpura; hemorrhages from mucous membranes; low platelet count; delayed bleeding time; relief of hemorrhage for three days followed transfusion; relief of hemorrhage after a spontaneous rise in the platelet count.

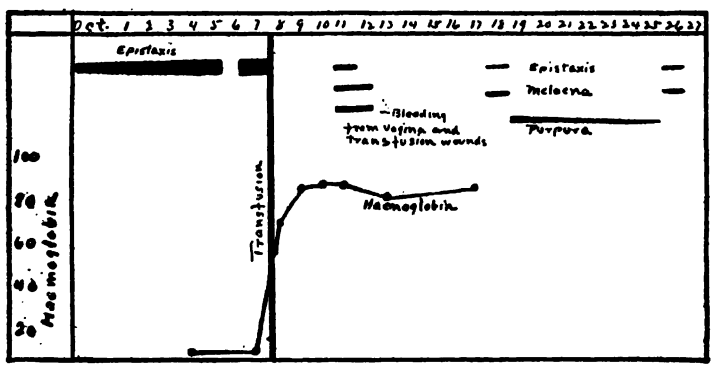

Fig. 7.—Chart of Case 3.

History.—Georgiana ——, American, a girl aged 3, was admitted to New York Hospital Oct. 3, 1909, complaining of epistaxis. The patient's parents, and three brothers and sisters are living and well. There is no history of hemophilia in the family. The patient has had no acute illnesses. She has had prolapse of the rectum several times. Since the age of 19 months, she has been subject to nose bleed, and ecchymosis following slight injury. Four months before admission to the hospital, symptoms were more severe, and at one time she became pale and weak from epistaxis and bleeding from a small cut on the head. She improved somewhat after this, and for the following two months there was little bleeding.

5. This case has been reported in another connection by Pool and McClure, Annals of Surgery, September, 1910.

Two days before she came to the hospital, epistaxis began again and continued until admission to the hospital.

Examination.—The patient was a moderately developed and nourished little girl. She was pale and rather weak from loss of blood. On the right shoulder, cheek, and lower extremities were several small ecchymoses. There were no telangiectases. The physical examination was otherwise unimportant. Epistaxis continued almost without ceasing for five days, and the child became almost pulseless.

Transfusion.—She was transfused on October 7 by Dr. R. D. McClure. The patient's father was donor.

Course of Disease.—Transfusion improved the patient's pulse—volume and color, but owing to bronchopneumonia, which developed at about the same time, her condition remained serious for a few days. The temperature, which had ranged from 98 to 102 F., began to decrease and reached normal about a week later. The pulse-rate immediately dropped from 160 to 120 and a few days later to 90, where it remained. There was no bleeding for three days after transfusion. On the fourth day there was slight epistaxis, and hemorrhage from the vagina and transfusion wounds. Later, she had slight epistaxis and melena, as marked on the chart, and a fine petechial rash which followed straining at stool.

Blood Examinations.—August 8—red cells 2,300,000, hemoglobin 84 per cent. Other estimations showed about the same ratio between the red count and hemoglobin. The white count varied from 16,000 to 21,000. Blood smears on some occasions showed an excess of lymphocytes (71 per cent.), but usually polymorphs predominated. The red cells showed polychromatophilia and moderate variation in size. There were no blasts. The coagulation time was about normal (Boggs' instrument). The urine was not remarkable.

For five weeks after leaving the hospital the patient had no further bleeding. During the sixth week, however, she had prolapse of the rectum with bloody stools. One week later, she noticed that ecchymoses followed slight injuries. When seen at this time, (Nov 24, 1909), her color and general health were fairly good. On her head, elbow and legs, were several small ecchymoses. Blood plates, as determined from stained smears and counting chamber, were extremely scarce. The bleeding time was about sixty minutes. The coagulation time was normal. The clot was firm and non-retractile. The white count was 7,000; polynuclears, 45 per cent.; lymphocytes, 55 per cent.; hemoglobin, 90 per cent. The patient was seen again four months later (April 7, 1910). She had been free from hemorrhagic symptoms for some time. Plates were then abundant in stained smears, and hemorrhage from ear

pricks would last for from five to ten minutes. The hemoglobin was 85 per cent.

Platelet counts were not made in this case at the time of transfusion. It seems probable, however, that, as in the previous cases, the relief of hemorrhage, after transfusion, was associated with an increase in the platelet count.

COMMENT

A review of the cases shows a striking dependence of hemorrhagic diathesis on the reduced number of platelets. In Cases 1 and 2 the platelet counts before transfusion were 3,000 and 20,000; the bleeding times were, respectively, ninety and twenty minutes. After transfusion the counts were 110,000 and 89,000, and the bleeding time in each case was three minutes. After the disappearance of these platelets, apparently introduced into the patients' circulation by transfusion, the bleeding times were again delayed (forty minutes and twenty minutes). In Cases 1 and 3 the bleeding times (forty minutes and one hour) came to normal after spontaneous rises in the platelet counts.

As to spontaneous hemorrhages, there was complete relief in Cases 1 and 3 for three days after transfusion and after spontaneous rises in the platelet counts. In Case 2 intestinal hemorrhage was slightly increased by transfusion, in spite of the fact that the general tendency to bleed (shown by the shortening of the bleeding time) was less marked. This apparently contradictory result may be accounted for by the fact that intestinal hemorrhage in this case was not entirely pathologic hemorrhage, but was due largely to bleeding from intestinal ulcers. The increase after transfusion may have followed the more complete filling of the blood-vessels.

In each of the cases the coagulation time of the blood bore no relation either to the platelet count or to hemorrhagic symptoms. The coagulation time was practically the same before and after transfusion, and before and after the spontaneous rises in the platelet count.

Other cases of hemorrhagic disease with a reduced number of platelets (twenty) have been reported by Denys, Hayem, Ehrlich, Helber, Bensaude and Rivet, Coe, Pratt and Selling. In one case reported by Bensaude and Rivet[6] there was a low count (6,000) during a hemorrhage crisis. During a remission in the disease the count was 161,000. Coe[7] has attached more importance to the relationship between the reduced number of platelets and hemorrhage than other observers. In one of his cases, the most severe epistaxis occurred when the platelets, estimated from stained smears, were almost absent. Previously they had been present, but in diminished number. In another case of purpura hemorrhagica, platelets, frequently estimated from smears, were almost absent during two hemorrhagic periods, and were present during remissions.

The reported cases differ in etiology. Many belong to the group known as idiopathic purpura hemorrhagica. Some of the cases were evidently symptomatic. One of Pratt's cases[8] accompanied nephritis. The platelet count was 9,000. Benzol poisoning was the etiologic agent in Selling's cases. The clinical condition was aplastic anemia. In one of his cases the platelet count was 2,500. In Case 2 reported in this paper, the hemorrhagic diathesis may have been secondary to ulcerative colitis. Platelet counts may also be low in lymphocytic leukemia, pernicious anemia, and early typhoid fever, and in each disease purpura hemorrhagica is a recognized complication.

The data leads one to believe that a reduced number of platelets is not simply a phenomenon accompanying some types of hemorrhagic disease, but rather that it may be the direct cause of hemorrhagic diathesis in several diseases.

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6. Arch. gén de méd., 1905, I, 193.
7. Coe, J. W.: The Treatment of Purpuric Conditions and Hemophilia, THE JOURNAL A. M. A., Oct. 6, 1906, p. 1090.
8. Osler's Modern Medicine, 1908, iv.

EXPERIMENTAL WORK

Experimental work seemed desirable to determine whether the hemorrhagic diathesis was due directly to the lack of platelets, or whether it was due to an abnormal coagulability of the blood which might accompany a reduced number of platelets. It seemed desirable also to know to what extent the platelet count must be reduced to cause hemorrhage.

In benzol poisoning we have a condition simulating idiopathic purpura hemorrhagica. Santessin[9] has reported cases and experiments in which hemorrhages were produced by benzol. Selling's cases[10] of a similar nature clinically, had very low platelet counts. He has found[11] that subcutaneous injections of benzol in animals reduces the platelet count. This reduction is thought to be due largely to the aplastic condition of the bone-marrow caused by the poison.

My experiments were performed mainly on dogs, and, according to a method suggested by Dr. Selling. Benzol was given daily for six to twelve days. The platelet count would usually rise at first, but later would fall and continue low for a number of days after the injections of benzol had been stopped. In several instances the count was reduced to 30,000. The white count was usually high even in the late stages of the poisoning.

The results[12] support a conclusion which might be drawn from this series of cases, namely, that when other conditions are normal, moderately low platelet counts are not associated with hemorrhagic diathesis. The platelet counts, after transfusion, in Cases 1 and 2 were only one-third of the normal, and yet there was no evidence of pathologic hemorrhage. The bleeding

9. Santessin: Arch. f. Hyg., 1897, xxi, 336; Skand. Arch. f. Physiol., 1900, x, 1.

10. Selling: Bull. Johns Hopkins Hosp., 1910, xxi, 32.

11. Unpublished experiments which will appear in the Journal of Experimental Medicine.

12. A complete report of results will be made later.

time was only moderately delayed (ten to twenty minutes) in Case 2, when the platelet counts varied from 20,000 to 30,000. The tendency to bleed in Cases 1 and 3 was extreme only during the practical absence of platelets. In the experimental work the platelet counts in dogs and rabbits were reduced from the normal (200,000 to 600,000) to from 50,000 to 75,000 without the appearance of hemorrhagic diathesis. Only a more extreme reduction (to 30,000) caused a delay in the bleeding time, and hemorrhages into the organs. There is an analogy between this observation and the observations of Whipple and Hurwitz on chloroform poisoning.[13] They found that, when other conditions are normal, a moderate reduction in the quantity of fibrinogen does not cause hemorrhagic diathesis. In their experiments hemorrhage was prolonged only when the reduction was extreme. It seems likely, then, that both platelets and fibrinogen play a striking rôle in the control of hemorrhage. Either one may be moderately reduced without symptoms, but after an extreme reduction there is a tendency to bleed.

The experiments failed to show abnormalities in the coagulability of the blood accompanying low platelet counts, which account for prolonged hemorrhage. The coagulation time was normal, or slightly shortened when the platelet count was as low as 30,000. The quantity of fibrinogen was normal or slightly increased (0.55 per cent. to 0.65 per cent.); furthermore, the fibrinogen present was all convertible into fibrin, and the fibrin examined in a number of ways had a normal microscopic appearance.

The serum in one instance was examined by Professor Howell, and found to contain thrombin. The only abnormality in the clot noted was diminished retractibility, a peculiarity shown by Hayem and others to be associated with and probably due directly to a lack

13. Unpublished experiments which will appear in the Journal of Experimental Medicine.

of platelets. Normal plasma deprived of platelets in various experimental ways clots quickly, but does not retract from the sides of the vessel containing it, and extrude serum.

The hemorrhagic diathesis is explained, possibly, through investigations on experimental thrombi. In a bleeding vessel, there are conditions suitable for the formation of a thrombus, that is, injured intima and a flowing stream of blood. Platelets, although they have little, if any, influence on the clotting of still blood, play a striking rôle in the formation of thrombi. The investigations of Hayem, Eberth and Schimmelbusch, Welch, Pratt, and others, have shown that after trauma to a blood-vessel platelets are the first element to adhere to the injured intima, and that within a few minutes they are massed in great numbers at the injured point. Later, leukocytes, fibrin, and red cells are included in the process, and a plug is formed consisting of masses of each of these elements. The investigations of J. H. Wright[14] show more clearly the rôle which the thrombus plays in stopping hemorrhage. His experiments were made by puncturing vessels with a needle. The resulting thrombi were likewise made up largely of platelets, and were evidently a factor in plugging the opening. An absence of platelets would lead to abnormality in the formation of thrombi, and might be a cause of prolonged hemorrhage. Pratt has laid more emphasis than other observers on the rôle which red cells play in thrombus formation. The failure of erythrocytes in carrying out this function explains, possibly, the delayed bleeding time noted in severe anemia.

CONCLUSIONS

The question now arises whether the facts admit the conclusion that an extreme reduction in the number of platelets is a cause of hemorrhagic diathesis, or whether the low platelet count must be considered a phenomenon

14. Personal communication.

which is sometimes found in hemorrhagic disease. The facts are as follows:

1. In the cases of hemorrhagic disease summarized, evidently differing in nature and etiology (acute and chronic idiopathic purpura hemorrhagica, chronic ulcerative colitis, aplastic anemia, nephritis), the constant features associated with the tendency to bleed were the reduced number of platelets, and the modification of the clot probably dependent on it, namely, diminished retractility.

2. In the cases reported in this paper, relief of the tendency to bleed followed not only the rises in the platelet count occurring at a remission in the disease, but followed also the rise brought about by transfusion. In the latter case, the tendency to bleed returned when the platelets disappeared.

3. Experiments in which the platelet count was reduced by benzol failed to show an abnormality in the coagulability of the blood, which accounts for the hemorrhages of benzol poisoning.

4. The structure and the mode of formation of experimental thrombi suggests, from an anatomic standpoint, that platelets play a rôle in stopping hemorrhage.

It may be permissible to mention two more points of interest suggested by the cases.

None of the patients showed so marked a tendency to bleed after transfusion as before, even after the platelet counts had dropped to their previous low level. In Cases 1 and 2, the bleeding times were ninety minutes and twenty minutes before transfusion. On the fifth day after transfusion, when the count was again low, the bleeding times were only half as long, fifty minutes and ten minutes. The spontaneous hemorrhages in Cases 1 and 3 were never so severe after as before transfusion. Since anemia is associated with a delayed bleeding time, this relief might be accounted for by the rise in the red count. In interpreting the beneficial results

following transfusion, this point should always be considered.

In each of the cases, the platelets introduced by transfusion disappeared rapidly. It is granted that these platelets may have been destroyed prematurely by the disease from which the patient suffered, or by processes analogous to hemolysis, etc. The uniform rapidity in the rate of disappearance, however, suggests that platelets are short-lived bodies. This interpretation is supported by the results obtained from the study of transfusion in benzol poisoning. In this case also, platelets introduced by transfusion disappear rapidly. It is also supported by results, to be reported later, which show that the normal rate of formation of platelets is probably extremely rapid, and may amount to as much as one-fourth of the entire number in the body per day. The evidence suggests strongly that platelets disintegrate or are utilized by the body in enormous numbers, and that the count is kept constant under a given set of conditions by a correspondingly rapid rate of formation.

The type of hemorrhagic disease described in this paper can be sharply differentiated from other types of disease, such as hemophilia, melena neonatorum, purpura simplex, Henoch's purpura, etc., which are due to other abnormalities. To this type of disease belong the so-called idiopathic purpura hemorrhagicas, and some cases of symptomatic purpura. The latter will probably be found most frequently in aplastic anemia, pernicious anemia, lymphocytic leukemia, typhoid fever and intestinal diseases. The symptoms may be mild, or may be so severe and acute that the patient bleeds to death in a few days. In mild cases, purpura may not appear. The only demonstration of the disease may be (as in Case 2) excessive hemorrhage from a local lesion.

The diagnosis is easy. If the platelet count is reduced to a sufficient degree to cause hemorrhage, the fact may be determined by examining carefully made cover-glass

preparations. The absence of retractility of the clot is considered by Hayem and his pupils characteristic of the condition, and is of diagnostic import. A point which I have found of value in following the cases and also in the diagnosis is the marked delay in the bleeding time.

Transfusion gives good results in the treatment of the disease. In addition to replacing blood, it stops hemorrhage for a few days, and may tide the patient over a serious crisis. The treatment is probably applicable to the symptomatic as well as to the idiopathic types of disease, and may be useful in the treatment of some cases of typhoid hemorrhage.

In concluding, I wish to acknowledge my indebtedness to Dr. E. H. Whipple, of the department of pathology, to Professor W. H. Howell of the department of physiology, and to Dr. L. Selling for their kind assistance in the experimental work.

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ABSTRACT OF DISCUSSION

Dr. J. H. Pratt, Boston: There seems to be some relation between the blood platelets in the blood and purpura hemorrhagica. Normally, the number of blood platelets is about 450,000 to the cubic millimeter. In simple purpura I found the platelet count was greatly reduced; in one fatal case it fell as low as 7,000. This patient had continuous hemorrhages from the lips and mouth. The platelet count was made 3 times on different days, and the largest number of platelets found was 16,000. In a case of mild purpura hemorrhagica there were 105,000 platelets per cm. The only other condition in which I have found very low platelet counts is lymphatic leukemia. The relation between purpura and the coagulation time is less clear. Wright asserted that purpura was due to delay in the coagulation time and that the treatment of the disease consisted in reducing the coagulation time to the normal by the administration of calcium chlorid or calcium lactate. I found the records of the Johns Hopkins Hospital and the Massachusetts General Hospital those of 34 cases of purpura in which the coagulation time of the blood had been determined. The average coagulation time of the blood in this series of cases was 5½ minutes, which is within the normal limits. In only a few cases did I find

a delay in the coagulation. I have seen a patient with purpura bleeding to death from the mucous membrane when the coagulation time was normal. Over the lobe of the ear at the site of the puncture a thick, moist clot formed, but blood continued to ooze from the wound for a long time. I believe that Dr. Duke's method of determining the "bleeding time" will be found to have great clinical value. In the case I have just cited in which the coagulation time was normal the bleeding time was doubtless greatly increased.

Dr. W. W. Duke, Kansas City, Mo.: Transfusion must be done by the direct method. Defibrinated blood is free from platelets and therefore in itself would not increase the count. There is a special indication for transfusion preparatory to operation in this condition. In addition to the usual results which follow transfusion, the tendency to bleed is diminished.

THE DIFFERENT FORMS OF MEDIASTINAL PLEURISY WITH REPORT OF THREE CASES

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DEFINITION

By mediastinal pleurisy, anatomically speaking, we understand, of course, an inflammation of the part of the parietal pleura which covers the mediastinum, the anterior as well as the posterior. But when we speak of mediastinal pleurisy as a clinical entity we differentiate it as a particular form of pleurisy, not merely because the mediastinal pleura happens to be inflamed, but because in certain clinical aspects it differs radically from ordinary pleurisy. This difference is, however, present only in those cases in which the inflammation of the mediastinal pleura leads to the formation of an encysted gathering of exudate between the mediastinum and the internal surface of the lung. In the following description I shall therefore confine myself to cases of this kind, with exclusion, for instance, of cases in which the inflammation of the mediastinal pleura is a pleuritis sicca, or, if exudative, occurs in conjunction with inflammatory changes in the rest of the pleura with free communication between the different parts of the pleural cavity.

It is owing to the proximity of the mediastinum and its organs that mediastinal pleurisy differs in symptomatology, in diagnosis, and in prognosis from ordinary pleurisy. The characteristic symptoms of mediastinal

pleurisy vary, however, according to what part of the mediastinal pleura is involved. A gathering of fluid in front of the right pulmonary peduncle does not give the same symptoms as one in front of the left, and both these forms of mediastinal pleurisy differ in their clinical manifestations from those produced by a gathering of fluid behind the pulmonary peduncle, which, on the other hand, is liable to give the same symptoms, no matter whether it is located on the left or the right side of the posterior mediastinum. We may therefore distinguish between three forms of mediastinal pleurisy: (1) pleuritis mediastinalis anterior sinistra, (2) pleuritis mediastinalis anterior dextra and (3) pleuritis mediastinalis posterior

It will be my endeavor in this paper to show the justification and the importance of such a distinction. But before I begin to discuss these different forms a few words in regard to the history of mediastinal pleurisy may be of interest.

HISTORY

The history of mediastinal pleurisy is somewhat difficult to trace because many cases have probably been described under the diagnosis of mediastinitis. As early as 1654 Sennertus[1] in his "Practica Medicina," in speaking "de mediastinal inflammatione," says that the same causes that produce pneumonia also produce mediastinitis ("Ideoque causæ, quae peripneumoniam et inflammationem pulmonum excitare solent, et hic locum habent"), that the cough in mediastinitis is at first dry, then loose with a bloody and yellow sputum ("Tussis in principio est sicca post humida, et rubra quaedam ac flava rejiciuntur, plurium tamen flavi coloris . . . "), and that the pulse is, as in pleurisy, hard and unequal ("Pulsus qualis pleuriticorum, durus et inæqualis").

1. Sennertus, Daniel: Practica Medicina: De Mediastini Inflammatione, 1654. Lib. I. Part II. Cap. XIII.

Brookes,[2] in 1765, seems to have been the first one to speak of the possibility of mediastinal pleurisy, as he, in discussing empyema, says: "There may, I own, be abscesses formed between the lungs and the mediastinum." In 1776 Van Swieten[3] described a case which might have been one of mediastinal pleurisy; a 20-year-old boy was seized with right-sided pleurisy which ended in suppuration with great oppression, and from the thirty-fourth day he expectorated large amounts of pus for ten months; at that time the pus gradually broke through the sternum and a pint of fluid could be injected through the fistula into the cavity, which seemed located between the ribs and the pleura. The patient at length recovered.

Andral,[4] in 1829, however, gave the first definite description of the autopsy of two cases of mediastinal pleurisy, one of which, *intra vitam,* had been diagnosed as a suppurative pericarditis.

Laënnec,[5] in his "Traité de l'auscultation médiate" of 1830, mentions having seen cases of gathering of pus between the inner edge of the lung and mediastinum; Chomel,[6] in his article on pleurisy in the "Dictionnaire de Médecine" of 1842, indicates the deep-seated pain behind the sternum as characteristic for the inflammation of the mediastinal pleura; Stokes and Bell,[7] in 1842, say, in speaking of pleurisy: "If the disease be mediastinic the sound is dull on striking the sternum." None of these authors give any report of definite cases.

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2. Brookes, R.: The General Practice of Physic, London, 1765, ed. 5, i, 278.
3. Van Swieten: Commentaries on Boerhaave's Aphorisms Concerning the Knowledge and Cure of Diseases, Transl., Edinburgh, 1776, ix, 100.
4. Andral, G.: Clinique médicale. Paris, 1829, ii, 522.
5. Laënnec, R. T. H.: Traité de l'auscultation médiate et des maladies des poumons et du coeur., Ed. de la Faculté de médecine de Paris, 1879.
6. Chomel: Pleurésie, Dictionnaire de médecine, Paris, 1842, ed. 2, xxv, 25.
7. Stokes and Bell: Lectures on the Theory and Practice of Physic, Philadelphia, 1842, ed. 2, ii.

Bouveret,[8] in his "Traité de l'empyème" of 1880, is the first one to point out that an encysted mediastinal empyema may be situated either in front or behind the pulmonary peduncle. He also reports a case in which the clinical diagnosis of chronic pulmonary tuberculosis was made, but in which the autopsy revealed an encysted purulent pleurisy in front of the peduncle (he omits to mention on which side of the mediastinum) with 300 or 400 gm. of pus. Bouveret is of the belief that this kind of encysted pleurisy might be susceptible of a correct diagnosis if, on close examination, an area of dulness is found near the edge of the sternum, and he concludes that, if an exploratory puncture gives positive result, a surgical interference might not be impossible.

In the last three decades, the following cases of left anterior mediastinal pleurisy have been reported: one by Richardière[9] in 1882, one by Pel[10] in 1884, two by Grancher[11] in 1892, who seems to have been the first one to diagnose this form correctly *intra vitam;* two by Velimirovitch[12] in 1892, one by Thoinot and Griffon[13] in 1896, one by Edelmann[14] in 1898, whose article has not been at my disposal, and who seems to describe his case as one of pleuritis pericardiaca, and one by Dodd[15] in 1899.

In a search through the literature no reports of pure cases of right anterior mediastinal pleurisy have been found. Two of the cases reported in this paper belong to this class.

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8. Bouveret, L.: Traité de l'empyème, Paris, 1880, p. 553.
9. Richardière: Pleurésie purulente enkystée; péricardite. Bull. Soc. anat. de Paris, 1882, series 4, vii, 199.
10. Pel, P. K.: Ein merkwürdiger Fall von Empyem. Berl. klin. Wchnschr., 1884, xxi, 113.
11. Grancher: De la pleurésie médiastine, Bull. méd., Paris, 1892, vi, 1171.
12. Velmirovitch, N.: Etude sur la pleurésie médiastine, en particulier chez l'enfant, Paris, 1892.
13. Thoinot and Griffon: Pleurésie purulente médiastine à pneumocoques, Bull. Soc. anat. de Paris, 1896, lxxi, 568.
14. Edelmann, M.: Pleuritis pericardiaca mit Dysphagie und Bradycardie, Post. med.-chir. Presse, 1898, xxxiv, 313.
15. Dodd, W. S.: Empyema, Sacculated, Between the Heart and the Lung. Med. Rec., New York, 1899, lvi, 515.

The following cases of posterior mediastinal pleurisy have been reported: two by Dieulafoy[16, 17] in 1896 and 1898, who was the first one to diagnose correctly cases of this form; four by Chauffard[18] in 1902, one by Breton[19] in 1905, two by Fernet[20] in 1909, and one by Lafforgue[21] in 1909. One of the cases reported in this paper belongs to this class.

Five additional cases of mediastinal pleurisy have been reported, one by Commandeur[22] in 1893, two by Silvestri[23] in 1897, one by Ughi[24] in 1902, and one by Salvestroni[25] in 1905, but the reports have not been at my disposal.

Other authors who have written on the subject of pleurisy have paid little attention to this particular form. Walshe,[26] of London, in 1854, mentions the inflammation of the mediastinal pleura and claims that it is often accompanied with serous infiltration of the cellular tissue of the mediastinum itself.

Wood,[27] in 1855, says:

The inflammation may be seated in the mediastinum . . . but there is scarcely a sign by which it could be certainly distinguished in this situation. The position of the pain and the absence of the peculiar signs of other diseases

16. Dieulafoy, G.: Pleurésie médiastine à pneumocoque, Presse méd., 1896, p. 281.
17. Dieulafoy, G.: La pleurésie médiastine, Clinique médicale de l'Hôtel-Dieu, Paris, 1898-99, iii, 1.
18. Chauffard, A.: Des pleurésies séreuses médiastines, Presse méd. 1902, x, 363.
19. Breton, A.: Erreurs de diagnostic: pleurésie purulente partielle, prise pour un aneurysme de l'aerte, Revue gén de clin. et de thérap., 1895, xix, 292.
20. Fernet: Deux cas de pleurésie médiastine, l'une purulente, l'autre gangréneuse, traités et guéris par la thoracotomie, Bull. Acad. de méd., Paris, 1905, series 3, liv, 181.
21. Lafforgue: Pleurésie médiastinale, et déviation de la pointe du coeur, Bull. méd., Paris, 1909, xxiii, 575.
22. Commandeur: Un cas de pleurésie purulente mediastine suraigué; perforation du poumon; mort, Province méd., 1803, vii, 115.
23. Silvestri, T.: Duo casi di pleurite mediastinica, Gazz. d. osp. Milano, 1897, xviii, 549.
24. Ughi, O.: Pleurite mediastinica saccata di destra (sarcomatosa od accompagnata a sarcoma) con fenomeni di ostacolato circolo nella cava discendente, Pisa, 1902.
25. Salvestroni, G.: Sindromi mediastinica nella pleurite callosa, Corriere san., Milano 1905, xvi, 514.
26. Walshe, W. H.: A Practical Treatise on the Diseases of the Lungs, Heart and Aorta, London, 1854.
27. Wood, G. B.: Practice of Medicine, Philadelphia, 1855.

might lead to probable inferences . . . sudden discharges of pus by expectoration sometimes occur, which may be conjecturally ascribed to the opening of such abscesses into the bronchi.

Donaldson,[28] in 1885, believes that the mediastinal variety may be diagnosed by local symptoms and says that the pain is very deep and perceptible at the middle of the sternum. Germain Sée,[29] in 1886, considers the diagnosis of mediastinal pleurisy impossible before the production of a vomica. Hare,[30] in 1899, in his admirable book on affections of the mediastinum, points out that "in the past, the term mediastinitis was frequently applied to an inflammation of those portions of the pleurae which form the lateral boundaries of this space . . . A pleurisy of this character is almost impossible to diagnose during life." Whitney,[31] in 1897, gives a very accurate description of the anterior mediastinal pleurisy, but fails to mention the posterior form. Detot,[32] in 1904, in an excellent article on partial pleurisies, gives a very good description of both the left anterior mediastinal pleurisy, closely following the one given by Grancher, and the posterior mediastinal pleurisy, in accordance with Dieulafoy's description. Wilson Fox,[33] Preble,[34] Wilson,[35] barely mention that a mediastinal pleurisy exists. In no other text-books and treatises that have been available to me is mention made of this form of pleurisy.

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28. Donaldson: Diseases of the Pleura, Pepper's System of Practical Medicine by American Authors, Philadelphia, 1885.
29. Sée, Germain: Maladies simples du poumon. Paris, 1886, p. 513.
30. Hare, H. A.: The Pathology, Clinical History and Diagnosis of the Affections of the Mediastinum Other than Those of the Heart and the Aorta, Philadelphia, 1889.
31. Whitney, H. B.: The Non-Tubercular Diseases of the Pleura, Loomis and Thompson's System of Practical Medicine by American Authors, New York, 1897.
32. Detot, E.: Les pleurésies partielles, Gaz. d. hôp., 1904, lxxvii, 1321.
33. Fox, Wilson: A Treatise on Diseases of the Lungs and Pleura, London, 1891.
34. Preble, R. B.: Pneumonia and Pneumococcus Infections, Chicago, 1905, 106.
35. Wilson, James C.: Diseases of the Pleura, Pepper's Text-Book of the Theory and Practice of Medicine by American Authors, Philadelphia, 1895, ii, 521.

Out of the eleven cases reported of left anterior mediastinal pleurisy seven are described with sufficient detail to give us a comprehensive picture of this form of pleurisy.

ANDRAL'S CASE 1.[36]—A man of 29, infected with tuberculosis, suddenly had an acute pain between the left breast and sternum with intense anxiety; the countenance was pale, the breathing short and hurried, the pulse hard and frequent. Six days later, a dulness was found between the left breast and the sternum, where respiratory murmur was absent and heart-sounds were weak. The dulness spread over almost the entire precordial region and Andral made the diagnosis of effusion in the pericardium. The patient died on the twenty-first day. At the autopsy, the pericardium was found normal, but immediately behind the sternum and the anterior ends of eight or nine left ribs was found a vast cavity formed entirely at the expense of the pleura; it was filled with thick pus and lined with thick false membranes which were studded with numerous tubercles. In discussing this case, Andral points out that there was not much dyspnea, except at the commencement, due to the intense pain, and that death was occasioned not by embarrassment of the respiration, but by the infection, tubercles having been found in most of the internal organs.

RICHARDIÈRE'S CASE.[9]—A woman had been sick for two months, complaining of constant oppression and attacks of dyspnea. On admission to the hospital, flat percussion-tone was found over the entire left anterior side of the chest with absence of breath-sounds and vocal fremitus and with distant heart-sounds. The oppression grew more intense and she died a month later suddenly. Autopsy revealed a pleuritic abscess containing 700 or 800 gm. of pus, reaching from the middle of the sternum to the left axillary line and completely surrounding the anterior and left side of the pericardium, which was the seat of an intense inflammation.

Pel[10] gives an excellent report of a case:

PEL'S CASE.—A man of 32 had never been sick until he contracted left-sided pneumonia four weeks before admission to the hospital, Jan. 1, 1884. He complained of pains in the chest and dyspnea. Physical findings were: Slight cyanosis, left side of chest bulging and its respiratory excursions dimin-

36. Andral, G.: Clinique médicale, transl., by D. Spillan, London. 1836, 581.

ished, apex-beat not perceivable, a flat tone anteriorly from the clavicle almost down to the costal margin, with absence of breath-sounds and of vocal fremitus; absolute cardiac dulness reaching 1 cm. beyond the right sternal line, heart-sounds distant, clear, and heard best at the right sternal line; posteriorly over almost the entire left side of the chest, flatness and absence of breath-sounds and of vocal fremitus. An incision was made between the eighth and ninth ribs in the left scapulary line and a large amount of pus escaped. The patient improved but slightly, the temperature remained high, he had a chill, the pulse was rapid, irregular, weak, fairly full. A week later, there was a distinct bulging of the precordial region, the apex-beat was not perceptible, the anterior area of flatness extended from the upper margin of the third left rib to 2 cm. beyond the right sternal line and 3 cm. beyond the left mammillary line. The outline of the flat area was triangular, no pericardial rub was heard and heart-sounds were barely audible. A diagnosis of pericarditis exsudativa purulenta was made. After an incision had been made in the third interspace outside of the parasternal line, about one and a half or two liters of yellow pus came out in a stream which was synchronous with the heart-action. The introduced finger felt the heart beating. The patient improved immediately, but nevertheless, he died three days later of pyemia. The autopsy showed that there was no pericardial effusion, but there were two separate encysted empyemas, one posteriorly which had been opened at the first operation and was in process of healing and the other on the inner side of the left lung, between the lung and the heart, surrounding the left heart and reaching from the second rib to the diaphragm.

GRANCHER'S CASE 1.[11]—An 11-year-old boy, when brought to the hospital, had the classical signs of a large effusion in the left pleura; posteriorly a flatness reaching to the spine of the scapula, with greatly diminished vocal fremitus and with very distant respiration below and bronchial respiration over the middle third of the left lung; anteriorly an area of tympanism below the left clavicle and, below this zone, a flatness which reached downward to the space of Traube, which was only slightly encroached on, and outward to the side of the chest, with diminished vocal fremitus and with bronchial respiration; the heart was displaced toward the right and the maximum of its pulsations was perceived at the right edge of the sternum. Although these symptoms would indicate a pleurisy with free fluid, Grancher made the diagnosis of left anterior mediastinal pleurisy for several reasons. There was no deformity of the thorax, *i. e.*, no enlargement of the left side of the chest, no dilatation of the left costal inter-

spaces, no deviation of the lower end of the sternum toward the left. The maximum dulness was noticed, not behind, but in front and extended one cm. beyond the right sternal line, and even on the manubrium sterni the percussion-tone was flat. Furthermore, the displacement of the heart was very exaggerated; there was also a deep cyanosis of the lips and a marked collateral circulation on the chest. Nevertheless, the dyspnea was but slight. As it thus was evident that it was the anterior mediastinum that had yielded to the pressure of the fluid and not the thoracic wall, Grancher concluded that the fluid was not free but encapsulated between the mediastinum and the lung. A puncture was made (Grancher does not mention where it was done) and 850 gm. of serous fluid were withdrawn. The patient recovered.

GRANCHER'S CASE 2.[11]—This also concerned a child. The diagnosis of pericarditis with effusion had been made because of an enormous bulging of the precordial region with dulness extending from the sternum to the left side of the chest; the child was almost blue and was in imminent danger of syncope as soon as it was moved in the bed. Grancher considered the dulness too extensive for a pericarditis and found that the heart-sounds were not so obtuse and distant as is usual in pericarditis; they were heard quite well, but with their maximum intensity at the right edge of the sternum. Therefore, without asserting the integrity of the pericardium, Grancher concluded that probably mediastinal pleurisy was present. Puncture was made in the left axillary line and 950 gm. of serous fluid were withdrawn. The heart came back to its normal position, the dyspnea disappeared in a few hours, and the child recovered.

THOINOT AND GRIFFON'S CASE.[12]—These authors have given an incomplete report of the case of a 45-year-old woman who was brought to the hospital on the fifth day of her disease, with the typical history of a pleuropneumonia of the left side. She suffered intensely from pain and dyspnea. Her countenance was pale and she was evidently deeply infected. There was distant bronchial respiration, Traube's space was sonorous, and the heart was hardly displaced. She died on the seventh day of her illness. At the autopsy a small collection of pus was found between the left lung and the anterior mediastinum; there were thick fibrinous membranes; the lower left lobe was consolidated. Pneumococci were found in the pus.

DODD'S CASE.[15]—This was one of a 57-year-old man who about a month before had had pneumonia of the left lower lobe and thereafter had developed the usual symptoms of empyema. Percussion in the front gave dulness from the third

left rib downward and from the edge of the sternum to the mammillary line, with absence of respiratory sounds; the apex-beat was closer to the sternum than normally; there was a place of tenderness as large as the end of a finger at the junction of the fifth rib and the sternum. Behind, there were dulness and absence of respiration-sounds from the seventh rib downward. Resection of the eighth rib was made in the midaxillary line and 250 c.c. of pus was exacuated. The patient improved only temporarily, the left lung gradually expanded, and vesicular breathing was heard to the base of the lung. But anteriorly, the only change to be found was that the apex-beat had returned to within half an inch of its normal position. He died twelve days after the operation from embolism in the left side of the brain. At the autopsy, an abscess with 300 c.c. of pus was found between the pericardium and the left lung and was in relation with the anterior wall of the chest only in the fourth intercostal space from the mammillary line for about 3 cm. toward the sternum. A needle in the fourth interspace, 1 cm. inside the mammillary line, would probably have found the abscess without entering the pericardium.

From the reports of these cases we find that the left anterior mediastinal pleurisy corresponds closely to ordinary exudative pleurisy in regard to etiology and pathology and to general symptoms, *i. e.,* those due to the infection. It is usually caused by the tubercle bacillus or the pneumococcus; the exudate is either serous or purulent, the latter being accompanied with formation of pseudomembranes. It is rare to find cases of left anterior mediastinal pleurisy without complications. Tuberculosis of other organs, a pericarditis, an empyema of another part of the left pleura, a pneumonia of the left lower lobe, an embolus of the brain are the complications which have been recorded in the reports of these cases.

The left anterior mediastinal pleurisy owes its distinctive features, of course, to the localization of the pathologic process. In some cases the entire height of the left anterior mediastinal pleura is affected; in other cases the pathologic changes are confined to the lower part of it. There is no case on record in which the inflammation has spread above or below the pulmonary

peduncle to the posterior mediastinal pleura, but in some cases the anterior median parts of the left diaphragmatic and parietal pleuræ have also been involved. At times the larger part of the exudate is covered by the anterior edge of the left lung, leaving only a small part of it in relation to the thoracic wall, underneath and close to the sternum, but usually, if the effusion is somewhat large, and particularly in case of a serous exudate, the edge of the lung is displaced more or less outward, exposing a larger part of the exudate.

Of the subjective symptoms the pain is the most characteristic one, being localized behind the sternum or between the sternum and the left breast; it varies greatly in intensity and is not always present. The degree of dyspnea, of oppression, of anxiety, seems to be more proportionate to the severity of the pain than to the amount of exudate. Thoinot and Griffon's patient suffered intensely from pain and dyspnea, although the amount of pus was small, while in Grancher's first case the dyspnea was very moderate, although the effusion measured nearly 1.000 c.c

The objective phenomena vary, of course, according to the size of the effusion. A small effusion will cause an area of flatness extending only from the left sternal line to the left nipple-line, with diminished or absent vocal fremitus and respiration-sounds over the flat area, with only slight or no displacement of the heart, and with no cyanosis. If the effusion is large, it may cause a bulging of the precordial region and the flat area may reach from several centimeters beyond the right sternal line to the left axillary line and upward to the second rib, and we may find a flat percussion-tone even over the manubrium sterni. In these cases the anterior mediastinum is more or less displaced to the right; the apex-beat may be seen close to the sternum, but is usually not perceivable; in several cases the heart-beat has been noticed at the right sternal line. As a consequence of the displacement of

the heart, more or less deep cyanosis may appear, but it seems to be of rare occurrence; only in one case was an engorgement of the thoracic veins noticed, the disturbance of the circulation being due probably to interference in the right auricle and the superior vena cava. To explain the cyanosis in cases of left-sided pleuritic effusion, as some authors do (Moxon[37]), as a result of pressure on the left auricle with subsequent stasis backward and dilatation of the right heart, seems scarcely to be accurate, as only the auricular appendage is covered by the left mediastinal pleura, and consequently liable to be exposed to pressure, while the rest of the left auricle is in relation to the organs contained in the posterior mediastinum. The respiration-sounds and vocal fremitus over the dull area are, as usually in pleurisy with effusion, diminished or absent. The heart-sounds are obtuse and distant and more clearly heard at right sternal line than to the left of the sternum.

The prognosis in left anterior mediastinal pleurisy is more serious than in pleurisy with free exudate because of the greater pressure to which the heart is exposed, and perhaps also because of greater danger of a complicating pericarditis or cerebral embolus.

In regard to the diagnosis of left anterior pleurisy the main difficulty is to differentiate it from an exudative pericarditis, from a pleurisy with free exudate, and from an anterior suppurative mediastinitis.

The differential diagnosis between exudative pericarditis and left anterior mediastinal pleurisy is no doubt difficult. "Handelt es sich doch hier," as Pel says, "um die Unterscheidung einer Pericarditis suppurativa interna von einer Pericarditis suppurativa externa." We find in both a precordial dulness or even bulging, an apex-beat located inside the left border of the dull area, or entirely absent, distant heart-sounds; the triangular

37. Moxon, W.: Lecture on the Difference between Effusion in the Right and Left Sides of the Chest. Lancet, London, 1884, i, 53.

shape of the dull area usual in pericarditis has been observed also in a case of left anterior mediastinal pleurisy; cyanosis occurs in both; the character of the pulse is of no assistance in making a diagnosis. There is, however, one sign which if present is characteristic for left anterior mediastinal pleurisy, as Grancher has already pointed out, namely, that the heart-beat is perceived with its maximum intensity and the heart-sounds are heard most distinctly near the right sternal edge. It indicates that the heart has been pushed toward the right by a pleuritic effusion and not removed from the proximity of the anterior chest wall by the interposition of a pericarditic exudate. Other signs may be of help for the diagnosis. A well-marked border-line between the flat area and the resonant area over the left lung speaks in favor of a pericarditis. The presence of Skoda's sign below the left clavicle, or of signs of congestion or of inflammation of the left lower lobe, or of signs of another encysted pleuritic effusion speak in favor of a mediastinal pleurisy.

Left anterior mediastinal pleurisy might be mistaken for a pleurisy with free exudate under two conditions. One of them is that, in addition to the left anterior mediastinal pleurisy, another encysted gathering of fluid exists in the lower posterior part of the left pleura; a puncture will then be made posteriorly and the fluid withdrawn, but the symptoms from the anterior part of the chest will remain unchanged and a correct diagnosis will be possible. The other condition is that, in a case of left anterior mediastinal pleurisy, the left lower lobe is congested and surrounded by a thin layer of fluid, as occurred in one of Grancher's cases; a correct diagnosis was here made, when by careful observation, admirable for its accuracy, it was demonstrated that it was the mediastinum and not the thoracic wall that had yielded to pressure from the fluid.

The differentiation of left anterior mediastinal pleurisy from anterior suppurative mediastinitis (Hare,[30] Christian[38]) also offers some difficulties, at least under certain conditions. When a mediastinitis is due to a trauma or to a sternal osteomyelitis or to a mediastinal lymphadenitis, the diagnosis might be quite clear; but, when, as occurs in rare cases, it is caused, through extension of the inflammatory process, by a pulmonary affection or by a pleurisy or a pericarditis, it seems hardly possible to arrive at a definite diagnosis.

A skiagram might be of service for diagnosing this kind of cases, but no mention is made of its use in any of the reports which have been published hitherto.

PLEURITIS MEDIASTINALIS ANTERIOR DEXTRA

While no reports of right anterior mediastinal pleurisy could be found in the literature, two cases of this kind have come under my notice.

CASE 1 (personal).—Adolph N., a tuberculous subject, aged 37, on June 12, 1906, suddenly became very sick, had a severe chill and a very acute pain which he located in the right side of the chest, especially between the sternum and the right nipple, and which made it extremely difficult for him to breathe. He was admitted to the Augustana Hospital June 18, 1906. Temperature 102, pulse 86 and respiration 24. His lips were dark blue; both head, neck, thorax and upper extremities were deeply cyanotic, and the veins in these regions were engorged. Amphoric breathing and large crackling râles were heard below the right clavicle. The percussion-tone was dull over the lower anterior part of the right lung, with distant breath-sounds of vesicular character and only faintly perceptible vocal fremitus. Over the posterior part of the right lung there was normal resonance and vesicular breathing. A dulness over the corpus sterni I ascribed to a dilatation of the right heart. Over the lower anterior and lateral part of the left lung there were signs of a small effusion, probably remaining from an attack of pleurisy he had had a year previously. The apex-beat could not be located.

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38. Christian, H. A.: Diseases of the Mediastinum, Osler's Modern Medicine, Philadelphia and New York, 1907, iii, 890.

During the following three weeks, I tried in vain to determine the locality of the effusion, of the presence of which I had no doubt. I made numerous punctures over the lower anterior part of the right lung, all with negative results. A consulting physician was called, but could find no evidence of a gathering of fluid. In the meantime the patient suffered agonies, was deeply cyanotic, was practically gasping for breath both night and day, had an extremely severe pain in his chest, which made frequent hypodermic injections of morphin necessary. He could not eat on account of the dyspnea. The temperature usually remained at about 98 or 99, but occasionally rose to 101 F.; the pulse was not very rapid, varying between 73 and 100 a minute; the respiration varied between 16 and 28 a minute.

Finally on July 13, finding a very narrow margin of flatness and total absence of breath-sounds and vibrations along the right edge of the sternum, I introduced the exploratory needle in the fourth right interspace about 1 cm. from the sternum and aspirated a syringeful of serous fluid. Dr. A. J. Ochsner was asked to operate, partly because I did not like to introduce a large aspirating needle where I had made the exploratory puncture, on account of the proximity of the heart, and partly because I considered a continuous drainage necessary to relieve the condition permanently. The operation was performed the same day. After the sternal end of the fifth rib had been resected and the pleura had been incised, the lower anterior corner of the lung was seen in the wound and was seemingly normal. A finger was introduced around the anterior edge of the lung and as soon as it was pushed down between the lung and the mediastinum, there was a gush of serous fluid, the amount of which was estimated at about 500 c.c.

After the operation the cyanosis rapidly disappeared and the dyspnea was greatly relieved. Unfortunately, however, the patient was so exhausted that he failed to pick up and died July 20, 1906, a week after the operation. Autopsy was not permitted.

CASE 2 (personal).—George G., aged 30, a laborer, was admitted to the Augustana Hospital March 18, 1908. He had been well up to March 15, when he suddenly became sick. On admission he complained of a moderate pain in the right side of the chest, coughed, but expectorated only some frothy mucus; at no time did he raise any typically pneumonic sputum. He had to sit up in bed to get air, and evidently suffered greatly from dyspnea. Temperature 103.3, pulse 156 and respiration 48. His lips were dark blue; both head, neck and upper extremities were deeply cyanotic, and the veins in the

cyanosed parts were engorged. The apex-beat was seen two finger's breadth outside the left nipple-line; a dulness over the corpus sterni I ascribed to a dilated right heart; the heart-tones were clear. The left lung was normal except that the respiration-sounds were increased. Over the entire front part of the right lung there was marked dulness, increasing downward, and also over the lower half posteriorly; the upper posterior half was resonant. The vocal fremitus was increased over the upper part anteriorly, slightly diminished below. Bronchial breathing was heard over the entire front part of the right lung, close to the ear over the upper part, and more distant over the lower.

On March 19 venesection on right arm was made, as it was thought possible that the cyanosis was due to dilatation and insufficiency of the right heart. A quantity of dark blood (300 c.c.) was removed; no improvement. March 20 an exploratory puncture was made in the fifth interspace, just outside the right mammillary line, also with negative result. The next day I made a second puncture in the same interspace, but inside the mammillary line, also with negative result.

March 23, his condition was practically unchanged, the dyspnea was very severe, the cyanosis deep and the pulse was at times irregular. On examination I found a small area close to the right sternal edge where the dulness was particularly marked, the breath-sounds were barely audible, and the vocal fremitus was totally absent. I had observed the same phenomena on the day of his admission, but explained it as being due to a dilatation of the right heart. As, however, no other signs of such a dilatation were observed, I became convinced that an effusion between the right lung and the mediastinum was causing both the displacement of the apex-beat and the cyanosis as well as flatness and absence of both fremitus and breath-sounds. The exploratory needle was therefore introduced for the third time, but now in the fourth interspace, between the parasternal line and the sternal edge. A turbid, yellowish fluid was obtained. The same day the patient was operated on by Dr. E. H. Ochsner. The sternal end of the fifth rib was resected and about 500 c.c. of fluid removed. The cyanosis soon disappeared after the operation and the dyspnea was gradually relieved. The draining fluid gradually turned into thick yellow pus, the wound granulated and healed, and on June 8, 1908, the patient was discharged after having made an uninterrupted recovery. I regret to say that no effort was made to ascertain what micro-organism was the cause of the pleurisy. I believe, however, that I am justified in saying that it probably was a case of primary

pneumococcus-infection of the pleura with secondary or simultaneous congestion of the lung.

SAINSBURY'S CASE.[39]—A case has been reported by Sainsbury which clinically resembled these two cases very much, but in which the autopsy showed a different pathogenesis. A woman, aged 62, had suffered from winter cough for some years. Six weeks before admission she had a chill, cough got worse, she became short of breath and lost flesh. There was marked cyanosis, enlargement of thoracic veins, orthopnea, dulness from top to bottom over right lung and evidence of fluid in the pleural cavity, but no displacement of the mediastinum or liver. The chest was tapped and 15 ounces of dark, sanguineous fluid withdrawn; no more would flow off by siphon action. The patient died a month later. The entire right pleural sac was found to be converted into a cavity with thickened, rigid, almost cartilaginous walls, filled with sanguineous fluid. The parietal and visceral pleuræ were equally affected and the mediastinum toward its dextral aspect shared in the thickening. The right lung was pressed upward, inward and backward and occupied a third or a fourth of its normal dimensions. Tracing the large veins from the root of the neck downward, their dilated channels were found to maintain their patency till at their confluence in the superior vena cava where they entered the mediastinal thickening. The constriction here was such that the channel was reduced to a narrow, slit-like aperture. The mediastinal sclerosis causing the constriction was similar in character to, and in no sense demarcated from, the general pleural thickening. The rigid-walled right pleural cavity could not have been under any tension from the fluid it contained, and it is more than probable that the exudation was a passive one from the congested intercostal veins, following but scarcely pressing on the receding lung, as its thickened capsule (peripulmonitis) contracted on the sponge-like tissue of the lung.

A report of a case of mediastinal pleurisy published by Ughi[24] has not been at my disposal, but judging from the title of the article—"Pleurite mediastinica saccata di destra (sarcomatosa od accompagnata a sarcoma) con fenomeni di ostacolato circulo nella cava discendente"—it seems to have concerned a case of sarcoma with obstruction of the descending vena cava, with effusion in the right anterior mediastinal pleura.

From the reports of these two cases of right anterior mediastinal pleurisy, it will be seen that they, in many

39. Sainsbury, H.: Chronic Right-sided Pleurisy with Constriction of the Superior Vena Cava Simulating Intrathoracic Tumor. Lancet, London, 1895, ii, 1359.

respects, showed a similarity with cases of left anterior mediastinal pleurisy. They were caused, one by tuberculosis, one by pneumococcus infection. In one of them the exudate was serous, in the other purulent. Most of the symptoms were like those caused by left-sided pleurisy: pain, most severe between sternum and right breast, dyspnea and oppression in proportion to the pain, a flatness along the right sternal edge and over the corpus sterni, a dulness over a smaller or larger part of the right lung, due to simultaneous congestion, absence of breath-sounds and vocal fremitus over a narrow flat area close to the sternum, and displacement of the heart.

In but one respect, I believe, the two cases of right anterior mediastinal pleurisy differed materially from those on the left side, namely, in regard to cyanosis, and this difference is sufficiently great, in my opinion, to form one of the reasons why the right and the left anterior mediastinal pleurisy should be distinguished as two different forms. In the two cases observed by me, the most striking feature was the cyanosis, which was extremely deep. Furthermore, the cyanosis was limited to head, neck, thorax and upper extremities and the veins in these regions were engorged. In Andral's and Thoinot's cases of left anterior mediastinal pleurisy, the countenance was pale; in Pel's case there was slight cyanosis; in Richardière's and in Dodd's cases no mention was made of the complexion and consequently one is justified in assuming that, if cyanosis was present, it was not marked. Only in Grancher's two cases was the cyanosis deep, and only in one of these were the thoracic veins dilated. Both concerned children with very large effusions.

It is only natural that cyanosis should be an early symptom in right anterior mediastinal pleurisy, when one considers that it is the right auricle and particularly its upper extension, the superior vena cava with its easily depressible walls, that are directly covered by the

right mediastinal pleura, and are the very first organs that will be exposed to pressure from an effusion gathering between the right lung and the anterior mediastinum. The intrathoracic part of the inferior vena cava seems to be too short and located too far backward to suffer from pressure from the exudate; at least in my two cases there were no signs of passive congestion below the thorax. On the left side conditions are somewhat different. An effusion gathering between the left lung and the anterior mediastinum will cause pressure on the right and left ventricles; but as their walls are rigid, no disturbance of the circulation will arise until the effusion becomes large enough to displace the heart considerably toward the right and thus cause, secondarily as it were, a pressure on the right auricle and the superior vena cava.

Another reason, however, for differentiating the right and the left anterior mediastinal pleurisy as two distinct forms, is the difference in their differential diagnosis. While either of them could be mistaken for a pleurisy with free exudate or a suppurative anterior mediastinitis, it is only a left anterior mediastinal pleurisy that could be coufounded with pericarditis and only a right anterior mediastinal pleurisy that could be confounded with a dilated right heart and with any disease causing a direct pressure on the commencement of the superior vena cava.

Right anterior mediastinal pleurisy and dilatation of the right heart both produce dulness over the sternum extending beyond the right sternal edge, displacement of the apex-beat toward the left, and cyanosis. It should not, however, be difficult to differentiate these two conditions because, when these three symptoms, dulness, displacement of apex-beat, and cyanosis are as pronouned as they were in the two reported cases and if they are due to dilatation of the right heart, other symptoms of dilatation must necessarily also be present, namely, epi-

gastric pulsations, tricuspid murmur, and venous pulse, symptoms which are not found in right anterior mediastinal pleurisy.

Any pathologic formation causing pressure on the superior vena cava may give symptoms similar to those of the right anterior mediastinal pleurisy; but particularly mediastinal sarcoma and carcinoma, aneurism of the aorta, and anterior suppurative mediastinitis should be differentiated from this form of pleurisy. The history of the disease, its mode of onset, as well as its course, the presence or absence of signs of infection, among which a high leukocytosis is of special importance, the presence of co-ordinate symptoms, are factors which, when carefully considered, should be sufficient to insure a correct diagnosis. The possibility of other mediastinal tumors or inflammatory products being present (Hare[30]) should be kept in mind, as a lymphadenitis, a mediastinal dermoid cyst, a syphilitic mediastinal gumma (Buttino[40]), a lipoma, a metastatic cancer, an endothelioma, a branchioma (Duret[41]), a chrondroma, a fibroma, hematoma, a fibrous infiltration, enlargement of mediastinal glands or of thymus, etc.

PLEURITIS MEDIASTINALIS POSTERIOR

Eleven cases of posterior mediastinal pleurisy have been previously reported.

ANDRAL'S CASE 2 (Cited from Dieulafoy[16]).—A 37-year-old man entered the hospital June 14, 1822, showing signs of pulmonary phthisis in the last stage. June 17 he had a vomica, expectorating a large amount of pus. He died July 8, 1822. At the autopsy, numerous tuberculous cavities were found in both lungs. There was a perforation the size of a pea of the posterior part of the right main bronchus, leading into a cavity which was large enough to admit an orange. This cavity was bounded exteriorly by the right lung, posteriorly by the ribs, interiorly by the spinal column and the posterior mediastinum, anteriorly by the right pulmonary vessels.

40. Buttino, D.: Di un caso di tumore sifilitico del mediastino, Riv. crit. di clin. med., 1908, ix, 1.
41. Duret, H.: Branchiomes malins du cou et tumeurs du médiastin, Jour. d. sc. med. de Lille, 1908, i, 217.

DIEULAFOY'S CASE 1.[18]—A 44-year-old woman caught a cold and had chills; next day she began to have a cough, which soon became paroxysmal and she was considered to have whooping-cough. After two months she became hoarse, a few days later stridor appeared, and she had violent attacks of suffocative cough, which was accompanied, if coming on shortly after a meal, by vomiting, and followed by the expectoration of a whitish, frothy suptum. Finally it became difficult for her to swallow. She entered the hospital three months after the beginning of her illness. On examination, no abnormal signs from the chest were found, the temperature was normal, but the larynx and the trachea deviated toward the right, the false vocal cords were edematous, there was no paralysis of the recurrent nerve. She gradually grew worse, the stridor became still more pronounced, the dyspnea was continuous. A week after her admission, she had a chill, followed by fever, and a few days later she had a vomica and expelled, during twelve hours, 200 gm. of yellow pus, which contained pneumococci. The diagnosis of posterior left mediastinal pleurisy was made. The symptoms gradually disappeared and the patient recovered.

DIEULAFOY'S CASE 2.[18]—A young, healthy man suddenly became sick with chills, oppression and dyspnea, which at first came on only on exertion, but soon became permanent and was aggravated by the slightest effort. A few days later he began to have fits of paroxysmal, dry cough, resembling whooping-cough, and at the same time his voice became husky. Four weeks later, deglutition became difficult and only liquids could be swallowed. Five weeks after the beginning of his illness, he was admitted to the hospital. A loud inspiratory stridor was heard, there was depression of jugulum and epigastrium at each inspiration, the veins of the upper part of the chest were dilated. At the level of the third and fourth vertebræ a small area of dulness was found between the scapula and the spine on the left side, over which area bronchial respiration and a few râles were heard. On the day after his admission he had a vomica and expectorated about 80 gm. of thick greenish pus. No bacteria were found, but the patient's blood-serum agglutinated penumococci. He gradually recovered completely.

BRETON'S CASE.[19]—A 47-year-old laborer, an alcoholic, in May, 1904, began to complain of palpitations and dyspnea on exertion, and shortly afterward of severe retrosternal pains and precordial angina with sensation of faintness and with vertigo. On his admission to the hospital in June, 1904, he was intensely anemic, had no fever, remained in dorsal position, in which his respiration was free, while any other posi-

tion caused oppression and dyspnea. Physical examination of the lungs revealed only a slight dulness close to the spine on the left side. The apex-beat was seen 1.5 cm. outside the nipple-line; palpation gave the impression of violent cardiac contractions; the closure of the aortic valves was accentuated and was heard also to the right of the spinal column; the pulsations in the crural arteries were asynchronous. Gradually a dulness in the aortic region appeared, slowly increasing and spreading along the right sternal edge, and, at about the same time, a murmur could be heard in the third right interspace which at first was single, systolic, soft, and afterward became double. Radioscopy showed a dark zone close to the left lateral aspect of the spinal column at the level of the mediastinum. The patient began to have a slight cough, but still no fever. The diagnosis of aneurism of the thoracic aorta was made. The patient gradually grew worse and in July, 1904, new symptoms appeared: cachectic discoloration of the skin, dilatation of the thoracic veins, hoarseness and dysphagia. The diagnosis of aneurism was abandoned for one of neoplasm of the posterior mediastinum. The patient died August 1, 1904, in extreme dyspnea. Three days previous to death the temperature was febrile.

At the autopsy a pleural abscess containing 300 or 400 gm. of yellow pus was found between the posterior mediastinum and the left lung, closely adherent to the descending aorta. The adjacent pulmonary parenchyma showed traces of subacute inflammation. The pericardium contained 200 gm. of serous fluid, the myocardium was hypertrophic, no valvular lesions were found and the aorta was normal, excepting a thickening of its membranes where it adhered to the abscess. Amyloid degeneration was found in the liver and kidneys.

Author's Case.—One case of posterior mediastinal pleurisy has come under my personal observation: Nils L., aged 35, a teamster, contracted pneumonia in April, 1897. After five days he began to improve, but after another week or two he gradually became worse again, had severe chills at irregular intervals, expectorated yellow pus, usually only small amounts, but a few times by the mouthful; in fact, so much that it came out both by nose and by mouth; he was losing in weight and the feet began to swell. When this condition had lasted about two months, I was called to see him. He was then emaciated, temperature 102, pulse 92, respiration 22 to the minute; he complained of slight dyspnea, but could breathe comfortably when in bed. There was dulness over the entire left lower lobe posteriorly; bronchial respiration was heard over the lower part of the scapula and the breath-sounds were faint and distant over the inner and lower parts of the left

lung posteriorly. The urine contained a small amount of albumin and there was a considerable swelling of the feet (beginning amyloid degeneration of the kidneys). A few days later, on closer examination, I found a narrow vertical zone parallel with and close to the spine, where the percussion-tone was flat and where breath-sounds and vocal fremitus were absent. An exploratory puncture was made in the seventh costal interspace, fairly close to the spinal column; yellow pus was obtained, which contained numerous pneumococci. The next day, after the patient had been anesthetized, two more exploratory punctures were made, more laterally and lower down than the first one, as it was thought advantageous, in order to insure free drainage, to have the opening laid as low as possible; but when the result was negative in both instances, a resection of the eighth rib was made, close to the spine and about 250 c.c. of pus emptied out of the encapsuled cavity. The wound gradually closed, the patient recovered and gained 50 pounds in weight in less than half a year. No symptoms of pressure on the mediastinum and its organs were present in this case.

Other Cases.—Chauffard[18] reported four cases of posterior mediastinal pleurisy with serous effusion. In none of them were there any pressure-symptoms. The diagnosis was based on the presence of a narrow, vertical dulness along the spine, with the usual symptoms of effusion. Exploratory puncture was made in three of them with positive results. All of the patients recovered spontaneously.

Fernet[20] reported two cases of posterior mediastinal pleurisy, both on the left side, one following after pneumonia and one after lung-gangrene. Both cases showed the general symptoms indicating the presence of a collection of pus, and this was located when an area of flat percussion-tone and absence of vocal fremitus was found between the inner edge of the scapula and the spine; in both cases the third and fourth ribs were resected close to the spinal column and a large amount of pus removed. In one of the cases the patient had a vomica of about 50 gm. of pus a few days after the operation. No symptoms of pressure on the posterior mediastinum were present in either of these two cases and it seems that, although it was chiefly the mediastinal pleura that was affected, the inflammation also involved the pleural covering of the interlobar fissure and of the diaphragm.

Lafforgue's case,[22] of which only an incomplete report is given, concerned a 22-year-old man who, when admitted, had high fever, did not cough and had no dyspnea. A week later the apex-beat was found two fingers' breadths outside the mammillary line, and another week later, signs of effusion

(dulness, egophony, bronchial expiration) were noticed over a longitudinal area to the right of the spinal column. A skiagram confirmed the diagnosis, but exploratory puncture gave a negative result. The patient gradually recovered, the dulness, etc., disappeared spontaneously and the apex-beat receded to its normal position. The author considered that both the anterior and posterior mediastinal pleura were affected in this case. In view of the fact, however, that exploratory puncture between the spine and the scapula was negative, one may be justified in doubting the correctness of the diagnosis.

Out of these twelve cases nine are of only moderate interest, as they give no symptoms of pressure on the posterior mediastinum. They were ordinary cases of partial, encysted pleurisy with a somewhat unusual localization between the lung and the posterior mediastinum. In their symptomatology and diagnosis they differed in no respect from an ordinary encysted pleurisy and their distinction as a special form would hardly be warranted if an encysted pleuritic exudate of the same localization were not liable, under other circumstances, by pressure on the posterior mediastinum and its organs, to produce symptoms which are radically different from the usual ones of pleurisy as exemplified by Breton's one and Dieulafoy's two cases. The reason why an encysted exudate between the lung and the posterior mediastinum does not, in all cases, produce pressure-symptoms is not quite clear. The amount of the exudate is evidently of only partial importance, as in one of Fernet's cases two liters of pus gave no pressure-symptoms, while in Breton's case only three or four hundred grams of pus produced very serious ones. Probably the occurrence of pressure-symptoms is dependent on how early the adhesions are formed and how deeply the exudate is situated. In both Dieulafoy's and Breton's cases the abscess was evidently remote from the surface, as the only superficial finding was a slight dulness between the scapula and the spine.

The posterior mediastinal pleurisy corresponds, just as does the anterior mediastinal form, to ordinary exu-

dative pleurisy in regard to etiology, pathology, and general symptoms and gives a distinctive clinical picture only when it produces pressure-symptoms on the organs contained in the posterior mediastinum. It might therefore be of moment rapidly to pass in review the anatomic relations of the pleura to these organs (conf. Potarca[42]).

After having freely opened the right side of the chest from behind, one can observe, underneath the mediastinal pleura, immediately in front of the spinal column, the right azygos vein with its upper part arching over the root of the right lung. Farther below, also directly in front of the spinal column, the lower part of the thoracic aorta is seen, which here passes in a slightly oblique direction from left to right. In front of the vertical elevation caused by these two organs, the pleura forms a depression and in front thereof the thoracic part of the esophagus is seen almost in its entire length. The right pneumogastric nerve passes on its way downward, after having crossed in front of the root of the right subclavian artery, here giving off its recurrent laryngeal branch, in the groove between the trachea and the esophagus and, lower down, behind the right bronchus to the posterior surface of the esophagus. The anterior boundary of the right posterior mediastino-pulmonary space is formed, from above downward, by the right bronchus, the right pulmonary vein, and the thoracic part of the inferior vena cava.

If we open the left side of the chest from behind, we shall find in front of the spinal column the left lower and the left upper azygos veins, the descending part of the aortic arch, the thoracic aorta, and, in front of its lowest part the lower end of the esophagus, which here passes obliquely from right to left. The left pneumogastric nerve passes on its way downward on the antero-lateral aspect of the transverse and descending parts of the aortic arch, here giving off its recurrent laryngeal

42. Potarca, J.: La chirurgie intra-médiastinale postérieure. Paris, 1898.

branch, and thereafter in front of and obliquely across the aorta and behind the left bronchus, to the anterior surface of the esophagus. The anterior boundary of the left posterior mediastino-pulmonary space is formed from above downward, by the left bronchus, the left pulmonary vein, the lower corner of the left auricle and the upper posterior part of the left ventricle.

Other organs contained in the posterior mediastinum are the trachea, the thoracic duct, and numerous lymphatic glands.

After this digression on the anatomy it will be easier to explain the pressure-symptoms observed in Dieulafoy's and Breton's cases.

In Dieulafoy's Case 1 the exudate caused paroxysmal cough by pressure on the left pneumogastric nerve, stridulous inspiratory dyspnea, edema of larynx and hoarseness by pressure on the trachea, which deviated toward the right, and, perhaps on the recurrent laryngeal nerve, and, finally, dysphagia by pressure on the esophagus.

In Dieulafoy's Case 2 the exudate caused paroxysmal cough by pressure on the left pneumogastric nerve, stridulous inspiratory dyspnea with depression of jugulum and epigastrium by pressure on the trachea, dysphagia by pressure on the esophagus, and engorgement of the thoracic veins by pressure on the left azygos veins.

In Breton's case the exudate seems to have exerted pressure almost exclusively on the thoracic aorta, resulting in retrosternal pain and precordial angina, palpitations, dyspnea on exertion, accentuated closure of the aortic valves, and hypertrophy of the left ventricle with the apex-beat displaced toward the left.

Posterior mediastinal pleurisy is always unilateral. In six of the twelve reported cases the left posterior mediastinal pleura was affected, and in five of these the exudate was purulent, in one putrid; the right posterior

mediastinal pleura was affected in six cases, and in all of these cases but one was the exudate serous.

The prognosis of posterior mediastinal pleurisy seems to be very much less serious than of the anterior, as, out of the twelve cases, only two ended fatally. In this connection it may be worthy of note that, out of the seven cases with purulent or putrid exudate, vomica occurred in not less than five, and that in two of these five cases thoracotomy was not found necessary, as the abscess gradually emptied itself completely through the air passages.

The diagnosis of posterior mediastinal pleurisy, in cases in which no symptoms of pressure on the posterior mediastinum are present, is based on the same principles as the one of any encysted pleuritic effusion. When symptoms of pressure arise, a differential diagnosis must be made between posterior mediastinal pleurisy and any disease which is liable to produce pressure.

I shall confine myself to the enumeration of such diseases: (1) abscess of the posterior mediastinum, whether due to trauma, foreign body, suppuration of glands, perforation of esophagus or trachea, or to an inflammation spreading from an adjacent organ as, a retropharyngeal abscess, a pulmonary abscess, a suppurative pericarditis, a vertebral osteitis, or to metastasis; furthermore, (2) hypertrophic glands, (3) aneurism, (4) gumma, (5) neoplasm.

In case stridor is present, a differentiation should be made, as Dieulafoy points out, from any tracheal lesion, whether intrinsic or extrinsic, which is liable to produce stridulous dyspnea, as intratracheal gumma, polyp, stenosis, pressure from cervical glands or from struma.

TREATMENT

The treatment of mediastinal pleurisy, whether anterior or posterior, differs in no way from the usual one of any encysted pleurisy except that the indication for

surgical interference comes earlier than in any other form. In order to be able to make a thoracocentesis or a thoracotomy at the proper moment, we should not hesitate to make not only one, but if necessary, several exploratory punctures to locate the exudate. No rule can be given as to where to introduce the exploratory needle. By minute physical examination we should try to determine where the maximum flatness is located, where the vocal fremitus is least perceptible, where the breath-sounds are most distant, where egophony is most pronounced, and introduce the needle in the outer edge of the area thus determined.

CONCLUSIONS

1. The clinical manifestations of mediastinal exudative pleurisy differ according to the part of the mediastinal pleura involved, and consequently according to the part of the mediastinum exposed to pressure.

2. For this reason three different forms of mediastinal pleurisy are to be distinguished: (1) pleuritis mediastinalis anterior sinistra, (2) pleuritis mediastinalis anterior dextra, (3) pleuritis mediastinalis posterior.

3. This distinction is justified, not merely from an anatomic point of view, but because it corresponds closely to clinical facts. Pleuritis mediastinalis anterior sinistra resembles very much exudative pericarditis. The most striking symptom of a pleuritis mediastinalis anterior dextra is a very deep cyanosis of head, neck, thorax and upper extremities. A posterior mediastinal pleurisy will, provided the exudate is deeply situated and is sufficiently large, cause inspiratory stridor and sometimes a deviation of the trachea by pressure on the trachea, dysphagia by pressure on the esophagus, engorgement of the intercostal veins by pressure on the azygos veins, and paroxysmal cough by pressure on the pneumograstic nerve.

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ABSTRACT OF DISCUSSION

DR. DELANCEY ROCHESTER, Buffalo, N. Y.: Although I have nothing to offer in the way of cases to report in support of Dr. Frick's position, I do not believe that such additions to the literature should go without some discussion. We owe him a great deal for his careful analysis of his cases and for the careful examination and the knowledge displayed in making the diagnosis and his confirmation of it by exploration and, whenever possible, by autopsy. The literature on this subject will be greatly added to; we shall all be required to look more carefully into these cases hereafter. When there is cyanosis and difficult breathing, cases that have heretofore been looked on as cardiac, can now be proved to be mediastinal pleurisy, a condition which can be relieved by operative procedures.

DR. FRANK SMITHIES, Ann Arbor, Mich.: Were any photographic findings registered in these cases?

DR. ANDERS FRICK, Chicago: No photographs were taken of the anterior mediastinal pleurisies. In a few cases of left posterior mediastinal pleurisy, however, skiagraphs were taken and they indicated a shadow or dark zone to the left of the posterior mediastinum. In these cases, also, there was dulness between the spine and the left scapula.

MAGNESIUM POISONING

A STUDY OF TEN CASES

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INTRODUCTION

The salts of the Glauber salt group are characterized by the difficulty with which their solutions are absorbed from the gastro-intestinal tract. The most important members of the group are the sulphates of sodium and magnesium.

Both Glauber salt and Epsom salt are easily soluble in water. When these salts are taken into the system in dilute form their solutions pass through both the small and large intestines practically unchanged, because the tendency to absorption is so slight that under these conditions the solutions are virtually non-absorbable and because the salts prevent the absorption of any water which was used to dissolve them. Such solutions passing unchanged through the entire bowel produce their effect in part by simply washing out its contents and partly by their local irritant action on the intestinal wall.

In 1884 Hay[1] showed that the tendency to absorption of Glauber salt is increased by raising the concentration of the solution, and when, in the course of his experiments on animals (the intestinal tract of which was free from fluid) he gave the salt by mouth, he found that large quantities of the dry salt produced no catharsis

1. Hay: An Experimental Investigation of the Physiological Action of Saline Cathartics, Edinburgh, 1884, Jour. Anat. and Physiol., 1883, xvi, 391 and 1884, xvii, 222.

whatever, while the same doses given in dilute solution invariably produced copious movements. The dry salt was gradually absorbed from the gastro-intestinal tract into the blood and was excreted by the kidneys.

Beginning with concentrated solutions of Glauber salt, Gummilewski[2] found that the addition of water steadily diminished the tendency to absorption. Continuing the dilution, he reached a point below which absorption was reduced to a minimum; from this point on there was practically no absorption down to solutions of 1 per cent. and less. With its slight tendency to absorption the dilute salt solution does not normally remain in the intestine long enough to allow an appreciable amount of the salt to be taken up; if, however, a Glauber salt solution cannot readily leave the bowel on account of mechanical obstruction, or because peristalsis is much diminished or absent, then even a dilute solution will undergo gradual absorption, and there will be no catharsis. In the normal bowel the degree of dilution of an active Glauber salt solution has no bearing on the efficiency of the catharsis produced, a 2 per cent. solution being as effective as a solution containing 5 per cent of the salt, provided, of course, a sufficient quantity of the solution is given in each case.[3]

The question whether or not these salts by their presence in the intestine are capable of abstracting water from the system is still undecided, the experimental evidence on this subject being contradictory. According to Schmiedeberg[4] it is very unlikely that such abstraction should take place under normal conditions. If it ever occurs, Schmiedeberg[5] thinks, it will be most likely to happen when the system contains an excessive amount of water, as in cases of general edema, ascites, hydrothorax,

2. Gummilewski: Arch. f. d. ges. Physiol. (Pflüger's), 1886, xxxix, 584.
3. Aubert: Ztschr. f. rat. Med., 1852, part 2, p. 225, Buchheim and Wagner: Arch. f. physiol. Heilk, 1854, xiii, 93.
4. Schmiedeberg: Grundriss der Pharmakologie, 1906, p. 413.
5. Schmiedeberg: Grundriss der Pharmakologie, 1906, p. 416.

pleurisy with effusion, etc. Certain experimental work which I have done on this subject is corroborative of Schmiedeberg's theory. The results of these experiments are to be published in a later paper, together with the results obtained from a quantitative experimental study of the absorption of Epsom salt given in varying concentrations.

The medical literature gives no information concerning the conditions governing the absorption of magnesium sulphate from the gastro-intestinal tract, but the histories in the cases of poisoning by the internal administration of Epsom salt and the results I obtained in my experiments both give evidence to the effect that magnesium sulphate closely resembles sodium sulphate in every particular relating to its behavior after ingestion. Theoretically, therefore, we should expect to find that concentrated solutions of magnesium sulphate are absorbed in part from the stomach and intestines into the circulation, and that when a sufficient amount of magnesium is present in the circulating blood at any one time magnesium poisoning will result.

When magnesium salts are injected into the blood of animals a very characteristic intoxication is produced.[6, 7] The pulse, at first somewhat accelerated, soon becomes slower and slower, until the heart stops in diastole shortly after paralysis of the respiration. The respiration is affected from the start. The reflex irritability is lost twenty minutes after the beginning of the injection and it may still be absent for an hour and a half after respiration has returned to normal. The peripheral motor nerve endings are paralyzed, but where recovery occurs voluntary movements return long before reflex irritability is restored; 0.3 to 0.5 gm. per kilo body weight, given intravenously, produces death in dogs.

6. Clessin: Ueber die giftige Wirkung der Magnesium Salze Diss., Würzburg, 1881.
7. Recke: Experimentelle Beiträge zur Kenntniss der Wirkung der Magnesia sulphurica, Diss. Göttingen, 1881.

Subcutaneous application produces qualitatively the same symptoms, but much larger doses are necessary to cause death. On section of the animals Recke[7] found subpleural ecchymoses and extravasation of blood into the pleural cavities.

The work of Meltzer[8] seems to indicate that magnesium salts may produce intoxication through cumulation. I, too, have found the excretion of magnesium sulphate through the kidneys to take place so slowly that if small doses of Epsom salt in concentrated solution are given at short intervals cumulative poisoning may result.

If magnesium absorbed into the blood in sufficient quantity was the cause of intoxication in the cases I shall describe we may expect these cases to show symptoms and autopsy findings resembling those obtained in animals by the intravenous application of magnesium salts.

Of the ten cases which I shall discuss seven are to be found in the literature; two of the other three cases I have observed personally; the third case I obtained from the records of the Massachusetts General Hospital.

REPORT OF CASES

CASE 1.[9]—J. A., 31, Italian, married, second pregnancy, was brought to the hospital on January 22 with a history of having had no movement of the bowels for three days. The patient looked very sick, her respirations were slow and labored, but both the temperature and pulse were only 100. From time to time she vomited yellow watery matter. The uterus, at full term, lay in the right side of the abdomen: it contracted regularly every ten minutes. The left side of the abdomen was puffed up by a distended intestine; there was no visible peristalsis. The examination of a catheter specimen of urine showed the following: Quantity 125 c.c., specific gravity 1,080, no albumin, no sugar. Two glycerin enemas low were given without result. An oil enema gave result from lower bowel. A high turpentine enema gave a good result, relieving the distention. Operation was done for

8. Meltzer and Auer: Physiological and Pharmacological Studies of Magnesium Salts, Am. Jour. Physiol., 1905-1906, xiv, 366.
9. Boston Lying-In Hosp. Rec., 1909, cxlvii, 198.

removal of an ovarian cyst. In the urine, which was submitted to me for examination, I found a total of 0.6620 gm. of magnesium, calculated as oxid, and corresponding to 1.95 gm. of magnesium sulphate.

It was impossible in this case to obtain a history of the patient before entrance. Undoubtedly she had been given Epsom salt by her physician, but on account of obstruction of the bowel by the ovarian cyst the salt solution was not permitted to pass out of the intestine; consequently absorption of magnesium sulphate took place. After absorption into the blood the Epsom salt tended to increase the obstipation by paralyzing the bowel.

CASE 2.[10]—H. M., 60, chore-man. Diagnosis, chronic bronchitis and emphysema with acute exacerbation; chronic myocarditis.

Patient on entrance passed 30 to 35 ounces of urine, the examination of which gave the following: Odor and color normal, acid, specific gravity, 1,022, albumin, slightest possible trace, sugar absent, no casts. April 14 to 15, the urine rose to 2,940 c.c.; on April 17, it fell to 1,860 c.c., and on April 18 to 480 c.c. On April 14 magnesium sulphate, 1 ounce in concentrated solution every morning was ordered.

April 16, the patient was much more comfortable as a result of rest in bed. He ran an irregular temperature, normal in the morning and up to 101 F., in the afternoon. There were many moist râles and squeaks in the lungs.

April 18 the following information was obtained from Dr. Marks, the junior house officer, and from the nurse in charge of the patient: The patient felt poorly the morning previous. He vomited his salts; his pulse was weak and irregular; he became progressively weaker. His respiration, affected from the start, became more and more labored, and finally resembled Cheyne-Stokes respiration without the periods of apnea. The patient was very cyanotic. His condition seemed so serious that he was placed on the dangerous list.

My attention was called to this case by Dr. Duke, one of the house physicians, who brought me a specimen of urine with a specific gravity of 1,070, and it was in answer to my inquiry regarding the case that I received the above history. I immediately advised the discontinuance of magnesium sulphate for this patient because I was led, from my experience

10. Mass. Gen. Hosp. Rec., 1909, decxvii, 71.

with Case 1, to suspect magnesium sulphate as being the cause of the high specific gravity of the urine. Fortunately the patient had received no salts that morning on account of his weak condition.

April 24 the heart action was less irregular; lungs still showed many coarse râles; temperature still slightly elevated; patient up without ill effects.

The chemical analysis of the 120 c.c. specimen of urine obtained, yielded 0.4813 gm. of magnesium calculated as oxid, and corresponding to 1.42 gm. magnesium sulphate.

In my opinion this case is one of cumulative poisoning produced by a partial absorption of the doses given on April 14, 15 and 16. The salt given on April 17 served to hasten the onset of the attack.

CASE 3.[11]—E. I. B., aged 26, milliner, diagnosis, tapeworm.

May 23, on entrance to the hospital patient's urine showed a specific gravity of 1,008, albumin, slightest possible trace, no sugar. Patient was put on liquids without milk, and was given 5 grains of calomel that evening.

May 24, the patient was given 7 ounces of Epsom salt. 1 ounce every hour and a half during the morning, with excellent result. No vomiting.

May 25, patient vomited two doses of the salt. There was nausea the rest of the day. Urine, specific gravity 1,029. albumin slightest possible trace. Stool, normal in color, formed, eggs and segments of tenia present.

May 26, patient vomited two doses of salt. She was allowed to rest as quietly as possible, with the hope of beginning treatment.

May 27, patient vomited her medicines; she refused all food and drugs, except teaspoonful doses of albumin water and was beginning to look worn and haggard. She was fed by rectum and given enemas of salt solution. These enemas she retained well.

May 28, all idea of treatment for worm was given up; patient vomited even water. Physical examination was negative except for acne, which appeared two days previously.

May 30, condition of pernicious vomiting continued. Patient was able to retain only teaspoonful doses of milk and lime water or albumin water, and she often vomited these. The vomitus was green and slimy. The patient looked pale and drawn. The pulse was good, the temperature normal. The patient was sleepy most of the time; she lay

11. Mass. Gen. Hosp. Rec., 1906, dcxl, 122.

with eyes closed and hardly seemed to notice what was going on. The nausea was unrelieved. Patient said she could not move her limbs; she thought she was paralyzed. The patient's face was puffy. She was restless and querulous during the night.

The urine was pale, slightly cloudy, specific gravity 1,013, slightest possible trace of albumin casts present. The urine seemed much diminished; patient thought she had not passed any urine for several days, but the nurses thought that she had passed some urine with her stools and when she discharged nutrient enemas.

May 31, at 5 a. m. the pulse suddenly became weak; a few minutes later the house physician found patient pulseless and of a dirty ashen color. The patient was conscious when the heart was merely fluttering. Death occurred at 6 a. m.

Autopsy (M. G. H., Pathological Records, 1906, p. 273; autopsy 1,694).—Pleural cavity contains a slight amount of pale fluid. Peritoneal cavity contains a moderate amount of pale fluid and several pale yellow fibrin clots. Stomach and small intestinal mucosa shows patches of reddening. Kidneys weigh together 320 gm. The epithelium of the cortical tubules is generally flattened, the lumen of the tubules is rather larger than normal. The interstitial tissue is edematous in places. The epithelium of the glomerular capsule is thicker than usual, but there is no evidence of a glomerulo-nephritis, and there is no increase in interstitial tissue. The appearance of the kidney suggests the action of some toxic substance.

This case is undoubtedly one of magnesium poisoning. Unfortunately the urine was not examined for the presence of the salt, but the specific gravity of the urine of May 25 tells the story. At entrance the urine showed a specific gravity of 1,008; on May 25 the specific gravity was 1,029, although the patient had been taking practically no food. On May 31, when nearly all of the salt had been excreted, the specific gravity was 1,013. I have no doubt that specimens with a much higher specific gravity were passed in the twenty-four hours following the voiding of the specimen which was obtained on May 25. This specimen was passed at a time when the excretion of the salt was just beginning. This is another case of cumulative poisoning.

CASE 4.—Under the title, "Epsom Salt as a Poison," C. Fraser[12] reports a most interesting case of magnesium poisoning. A boy, aged 3½ years, took 1½ ounces of magnesium sulphate, mistaking the salt for sugar. On account of the bitter taste he drank a little milk to wash it down. The child's mother found him soon after this retching and suffering much pain. He complained of great thirst, his bowels had not moved. The nausea and retching continued all day. At 7 p. m. the pain was very severe and vomiting began. The patient suffered great pain all through the night and vomited at frequent intervals. When Dr. Fraser first saw the child at 2:30 p.m. it was twenty-five hours after he had taken the salts. He found the boy in bed with his face pinched, his eyes sunken and the skin very pale. His mind was clear. Every 2 minutes he had a colicky attack which made him draw up his legs. Temperature 100 F., pulse small, 160. Respiration labored. His tongue was very dry, the papillæ standing out prominently. His thirst was intense. There had been no movement of the bowels in twenty-four hours. The patient had passed only a half ounce of urine in twenty-four hours. Physical examination showed the abdomen to be distended and rigid, and the skin hyperesthetic. Catheterization yielded ½ ounce of bloody urine, no albumin and no sugar, very acid. The patient was weak and was constantly growing weaker. He vomited every few minutes small amounts of greenish-yellow material without any characteristic odor. The bowels were constipated, temperature and pulse the same.

Next day, vomiting was incessant as before, no movement, no urine, pulse uncountable. The abdomen was so distended and tender that it was feared the boy had peritonitis. He was therefore admitted to the hospital for laparotomy. The child was now in complete collapse, his temperature was subnormal, his pulse 160, the abdomen rigid and retracted. Laparotomy was done and two pints of sterile blood-stained serum obtained from the peritoneal cavity. No cause for intestinal obstruction to be found.

The first twenty-four hours in the hospital the temperature was 100.6 F., pulse 170; child was very ill and restless; he vomited frequently; no flatus or feces were passed in spite of frequent enemas. The child complained of intense thirst. Considerable quantities of blood-stained serum continued to drain from the peritoneal cavity. The dressing was changed every four hours. The child became moribund, and albumin water, brandy and rectal salines were not retained.

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12. Fraser, C.: Lancet, London, April 24, 1909, p. 1174.

The second twenty-four hours the child was still moribund; pulse uncountable. Normal saline solution was infused into the subcutaneous tissue of the axilla, after which the child improved, obtaining some sleep. There was still some vomiting, which, however, soon stopped. Half grain of calomel was given every hour. Temperature 101.5 F. In the afternoon flatus and feces passed and again after an enema. Catheterization at 4 p. m. yielded 1 ounce of urine. Recovery now followed quickly.

In this case the action of the salt after absorption into the blood had caused paralysis of the intestine. The slow excretion of the salt was also responsible for the almost complete suppression of the urine, the salt, by its great affinity for water, preventing the excretion of water by the kidneys.

CASE 5.—Neale[13] reports the case of a boy, aged 15, who took 1 ounce of magnesium sulphate in concentrated solution on an empty stomach. The physician arrived after twenty-four hours. In the meantime the boy had had three small movements. A few hours after the dose he felt sick and vomited; this condition continued through the night. The next day he tried to work, but had to give up. The vomiting continued at intervals. When the physician came the patient was lying in an attitude of flexion; he was very cyanosed; from time to time he had severe attacks of tetanic spasms, affecting the right side of the face and the right arm. The urine was dribbling. The pulse was imperceptible. He frequently vomited greenish fluid material. His temperature was 105 F. The next day he was better; 40 ounces of urine were withdrawn by catheter. He was well in a week.

In this case there was evidently a paralysis of the sphincter of the bladder. The tetanic convulsions are an interesting symptom. Two of the ten cases showed convulsions.

CASE 6.[14]—A woman in Dundee, Scotland, took 4 ounces of Epsom salt in concentrated solution at one draught. Half an hour later she felt so ill that she sent for a physician. An hour later she died. There was no purging. These are all the facts obtainable in this case, except that death was certified to as due to paralysis from an overdose of salts. There was no inquest.

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13. Neale: Pharm. Jour., 1896, p. 235.
14. Brit. Med. Jour., 1891, ii, p. 490.

The cause of death as given in the physician's certificate suggests that there was motor paralysis in this case.

CASE 7.—Luff[15] reports the following case: A woman servant aged 20 was found on her bed in the morning. The bed had not been slept in. Death had occurred some hours before. The autopsy was negative except for the presence of a light-colored semifluid mixture of water and magnesium sulphate in the stomach. Death was stated to have been caused by syncope. There was no purging. The salts had been taken on an empty stomach. It was learned later that the young woman had purchased 1 ounce of Epsom salt the day before from a neighboring apothecary.

CASE 8.—Sang[16] reports the case of a woman of 35 who took 4 ounces of Epsom salt in warm water to bring on the monthly period. Immediately after taking the salts she felt a burning pain in the stomach and bowels. Her breathing became difficult, she had a choking feeling, also a sensation as if the power were leaving her legs. There was no vomiting and no purging. Her pulse was 98 F.; the pupils were dilated; at times there was slight twitching of the face, but complete paralysis rapidly ensued, the patient became comatose and died seventy-five minutes after taking the salt. The radial pulse was felt for two to three minutes after respiration had ceased. There was no autopsy.

This case is one of the most typical of the ten. It shows the paralysis of respiration in a truly classical manner; also the final complete motor paralysis. Like the third of my cases, the victim in this case spoke of a sensation as if the power were leaving her legs. If Patient 3 had lived longer motor paralysis would probably have developed in her case also. In connection with this case it is interesting to note that Lewin,[17] reporting Case 8 in his text-book on toxicology, expresses his doubt of its being a case of magnesium poisoning because the victim was not purged.

CASE 9.[18]—A boy aged 10 was given 2 ounces of Epsom salt for worms. The salt was partly dissolved and partly mixed in a cupful of water. Immediately after swallowing the mixture he staggered and fell. Half an hour later the

15. Luff: Brit. Med. Jour. 1891, ii, 490.
16. Sang: Lancet, London, Nov., 7, 1891, p. 1037.
17. Lewin, Lehrbach der Toxicologie, 1897, p. 99.
18. Christison: On Poisons, p. 574.

physician found him breathing slowly and with difficulty. The pulse was imperceptible and the boy was in a condition of collapse. He died in forty minutes. There was no vomiting or purging. The autopsy was negative.

This case is remarkable for the suddenness of the onset, which is strongly suggestive of rapid absorption from the stomach.

CASE 10.[19]—An old man who was rather a heavy drinker fell the victim of a practical joke. A number of his companions put a large quantity of Epsom salt into his beer. After he had drunk several pints he was suddenly seized with violent purging. He died forty-eight hours later. The autopsy showed the mucous membrane of the gastro-intestinal tract to be inflamed.

The victim in this case may have died in consequence of the violent purging alone.

CONCLUSIONS

In one of these cases only, that reported by Taylor, active purging took place. The victim in this case was given Epsom salt in several pints of beer; the beer served to produce a dilute solution which escaped absorption, and therefore caused powerful catharsis. In Case 3 there is said to have been a good result after the seven doses of Epsom salt, but probably the patient drank a sufficient amount of water with some of her doses of salt which so diluted the salt that it was not absorbed. The patient in Case 4 is reported to have had three small movements. In all the other cases there was no catharsis; the salt, which was taken in concentrated solution, caused paralysis of the bowel after its absorption into the blood. This paralysis was so marked in Cases 1 and 4 that laparotomies were performed.

In all cases there was also a diminution of the urine, which in some cases amounted almost to anuria. The effect on the urinary secretion is due to the presence of the salt in the blood and tissues. On account of its great affinity for water the salt converts a large part of

19. Taylor: Poisons, p. 4.

the body fluids into an Epsom salt solution, which, being itself excreted only very slowly, holds the water back and reduces or prevents the secretion of urine.

Among the symptoms observed the paralyzing effect of the salt on the respiration was very prominent; it was spoken of in six cases. Convulsions, described as tonic in character in Neale's case, were seen in Cases 5 and 8. Dilatation of the pupils was observed in Cases 4 and 8. Motor paralysis was seen in Cases 6 and 8, and paralysis of the reflexes seems to have been present in Cases 3 and 8. Vomiting occurred in about one-half the cases.

The most characteristic findings disclosed by operation or autopsy are patches of reddening on the mucosæ of the stomach and intestines and free fluid in the abdominal and pleural cavities (Cases 3, 4, 10).

Fraser's case (4) suggests one very efficient remedial measure, namely, infusion with normal saline solution. The saline infusion given the child undoubtedly saved his life. I think, however, that intravenous application is preferable to intramuscular or subcutaneous infusion, because the relief of the patient will be more prompt and the chances of saving life will be better. The fluid introduced probably acts by diluting the Epsom salt so as to render it less toxic; the more dilute solution is also excreted more rapidly by the kidneys. Meltzer's[20] experiments on animals suggests a specific antagonistic action to magnesium on the part of calcium salts. The intravenous or subcutaneous application of lime salts may therefore be of great value in the tratement of magnesium poisoning.

On account of its paralyzing action on the reflex centers of the cord Meltzer[21] has advised the subcutaneous use of magnesium sulphate in cases of tetanus.

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20. Meltzer, and Auer: Am. Med., 1905, x, 916.
21. Meltzer: Inhibitory and Anesthetic Properties of Magnesium Salts, Med. Rec., New York, 1905, lxviii, 965.

Such application should be made with the greatest care only. I can conceive of the remedy being quite as bad as the disease.

SUMMARY

1. Magnesium sulphate in bulk or in concentrated solution is absorbed in part, at least, from the gastro-intestinal tract into the blood.

2. If a sufficient amount of the salt is absorbed at a given time poisoning will result; of the ten cases reported six resulted fatally. The symptoms and autopsy findings in these cases agree very well with those obtained in animals after the intravenous application of magnesium sulphate.

3. On account of the slowness of its excretion from the system, magnesium sulphate, given repeatedly in concentrated solution, may produce poisoning by cumulation.

4. In normal conditions of the bowel magnesium sulphate, in proper dilution, is a valuable cathartic; Hunyadi water, for example, is practically a 3 per cent. solution of Epsom salt (magnesium sulphate 1.5 per cent., sodium sulphate 1.5 per cent.)

5. It is not wise to give magnesium sulphate indiscriminately in cases of so-called acute intestinal obstruction, because when peristalsis is much diminished or absent, and in cases of mechanical obstruction of the bowel, even dilute solutions will be absorbed, with consequent danger of poisoning.

6. In cases of suspected magnesium poisoning large quantities of normal salt solution should be given intravenously. Dilute solutions of lime salts given hypodermically may also be of benefit.

7. The subcutaneous use of magnesium salts to produce catharsis, as proposed by Wade,[22] is not only absolutely irrational, but dangerous.

374 Marlboro Street.

22. Wade: Med. and Surg. Reporter, 1894, No. 4.

ABSTRACT OF DISCUSSION

DR. PHILIP S. ROY, Washington, D. C.: Wolfgang Pauli of Vienna, about 1905, in discussing sulphate of magnesia and some of the other powerful purgatives called attention to their danger. Pauli says that the purgative action of sulphate of magnesia is due to its irritating and caustic action on the tissues, also to a rise in blood pressure. The ion relations of the sulphate of magnesia to protein are similar although not so powerful as those of the bichlorid of mercury. Pauli's article impressed on me forcibly that care should be used in giving the sulphate of magnesia.

DR. NATHAN ROSEWATER, Cleveland, Ohio: Magnesium citrate is the form of magnesium salt which I give when I wish to produce catharsis. I prescribe it in concentration equivalent to one and one-third ounces of the salt in from four to six ounces of water. In my experience of many years, I have never seen such effects as described by Dr. Boos. It seems to me that one of the cases he reported should be ruled out because the effect was so immediate; absorption can hardly take place so fast as is indicated in his description of the case. In the other cases too I think that the results must have been due to something else than the magnesium, perhaps to the condition for which the drug was given. In only one or two cases do I believe that the Epsom salts seem to have had anything to do with the poisonous results. I have had a large experience with the use of the salts of magnesium and I have never encountered any untoward effects whatever, and have preferred a concentrated solution. It would require more than the report of two cases to make me believe that this agent is a poison, instead of having merely been used in cases with a toxic or fatal ending.

DR. H. E. DUNLOP, Canton, Mo.: It has been my experience, as I am sure it has been of the majority of physicians present, that magnesium sulphate is not at all toxic, at least in the dose usually administered. Does not Dr. Boos believe that idiosyncrasy had much to do with the results reported in his paper?

DR. D. C. WALT, Little Rock, Ark.: Magnesium sulphate is a valuable agent because of its affinity for carbon which exists in all ptomain bodies. It seems to have the power of neutralizing the toxic value by drawing to its embrace the carbon which is the basic element in poisonous compounds, whether it is the CHNO or CHO group. Nature handles the animal economy on a general plan and that plan is modified or influenced by certain conditions. I dislike to hear anything said against magnesium sulphate because it is one of the most commonly used and cheapest drugs and also one of the most valuable in medicine to-day. With regard to the toxic condition, we must remember that in the snake and in the wasp

the toxic effects are based on natural laws, and the toxic effects are regulated by a relation to carbon. I have had a personal experience with this agent as well as in my practice. I have a chronic affection which has been diagnosed as epithelioma, and I have used magnesium sulphate every day for over five years.

Dr. Louis Leboy, Memphis, Tenn.: The report of these cases is extremely interesting and I think they are sufficiently numerous to warrant consideration. What has been stated does not strike me as being a plea to discredit the giving of magnesium sulphate by any means; we must remember, though, that there are certain cases which result unfavorably after the administration of this agent. There seems to be no question but that a solution of magnesium sulphate cannot produce any toxic effects unless the metal in some way unites itself with some other substance. Idiosyncrasy is not usually a question of concentration, but of substance. It seems that it is only when in great concentration that magnesium sulphate is injurious, so that this would seem to argue against idiosyncrasy as being responsible for the unsatisfactory results. On the other hand, I believe that there is very little general toxic action resulting from the administration of magnesium sulphate. The question then arises: Is there not some other toxic material linked with the magnesium and which is absorbed at the same time through the intestines? That would be my interpretation of the cases reported by Dr. Boos. I should say that his cases were the unusual ones; possibly there was an incompletely digested material, or possibly the production of some ptomain substance, which was absorbed and thus caused the poisonous effect. These possibilities must be borne in mind and the report of but one or two instances of supposed poisoning from the administration of sulphate of magnesium should not be accepted as a statement that this is the sole poisonous agent.

Dr. John D. Reid, Pilger, Neb.: I should like to report a case which came to my attention last month, but which was not in my practice. The wife of a blacksmith had not been feeling well for several hours. Thinking that it would do her good, the husband gave her a dose of Epsom salts. Within one hour the woman was dead, whether from magnesium poisoning or not I do not know. Her husband was arrested for murder and the preliminary trial is to be held soon.

Dr. W. H. Philp, St. Francis, Ark.: These reports of deaths from the administration of common, everyday salts are interesting, and recall to my mind the case of a woman who was operated on for a minor gynecologic condition. Two or three days afterward she was given a small dose of salts, not more than 4 drams, and she was dead in one and a half hours, after having just such a set of symptoms as Dr. Boos has described.

The case was then recognized as one of magnesium poisoning, but this is the first time it has ever been reported.

Dr. George R. Neff, Farmington, Iowa: I have been using magnesium salts for years, and have never been so successful with them as I have during the last five or six years. I use magnesium internally and externally and expect to use it eternally. I think the sulphate of magnesium is one of the best agents we can use externally for the relief of pain, especially when used with phenol in the proportion of water 16 ounces, salts 1 ounce, phenol 10 drops. In the pleuritic pains in pneumonia, for instance, if this mixture is applied over the chest there are good results. In a knee joint affected with rheumatism, its action is like magic. Think of giving 7 ounces of sulphate of magnesia at one dose! Why should we not get toxic effects from such dosage? It should be remembered that we get toxic effects from medicines, just in proportion as carbon is contained in them. The more carbon the more toxic they are. Epsom salts are eliminative, given in proper doses. Take a case of bronchitis with a continuous hacking cough, and distress; using the following prescription, Epsom salts 3 drams, saccharin 3 grains, tincture of peppermint 10 drops, water 3 ounces, one teaspoonful every hour, the finest results are obtained. It will loosen the dry hacking cough and make a free discharge of mucus and all the symptoms will be relieved. If I had to make a choice of one medicine alone in the whole materia medica today, I would choose Epsom salts.

Dr. William F. Boos, Boston: I wish it to be distinctly understood that I would not have physicians discontinue the use of magnesium sulphate; I think it is one of the best drugs for the hospital, because it is cheap and efficient in action. But the salt should be given in proper form. Whenever magnesium sulphate is given in greater concentration than 6 or 7 per cent. it is absorbed in part and may produce intoxication. In one case in which the 24-hour urine was examined after the patient had received 1 ounce of magnesium sulphate dissolved in 3 ounces of water (a 33.3 per cent. solution), the urine was found to contain 104 per cent. more magnesium, calculated as oxid, than was normally present. In another instance in which Epsom salt was given in 13.3 per cent. solution, that is, 1 ounce magnesium sulphate in 6 ounces of water, the urine contained 60 per cent. more magnesium than normally. When, however, magnesium sulphate is given in 5 or 6 per cent. solution, that is, ½ ounce magnesium sulphate to 9 ounces of water, there is catharsis and none of the salt appears in the urine.

The last case I reported is probably not one of uremia, because the convulsions in uremia are clonic and not tonic in character. In one case the specific gravity of the 3-ounce specimen was 1,070, it was free from sugar and it contained

the equivalent of 1.4 grams of magnesium sulphate. There is no doubt that this was a case of magnesium poisoning and that the high specific gravity was due to the Epsom salt. It is only when we find an excess of magnesium in the urine that we can be certain that the salt was absorbed into the blood and that it was the cause of the intoxication. When the specific gravity of the urine is 1,070 or 1,080, as in the cases reported, or when it is above 1,030 in sugar-free urines generally, this form of intoxication should be thought of. It was only by accident that I found there was such a thing as magnesium poisoning. Magnesium sulphate was injected into the spinal canal by a man in Boston; the patient recovered consciousness about twenty-four hours later. I think it has not been given since. To produce intoxication this agent must circulate in sufficient quantity in the blood. In the cases enumerated, it was absorbed into the blood from the gastro-intestinal tract, and the effect is the same as when it is injected intravenously; in both cases we get symptoms typical of magnesium poisoning. Magnesium sulphate should be given well diluted; 1 to 18 is the proper dilution; that is, ½ ounce of the salt dissolved in 3 ounces of water, followed immediately by a glass of water. Such administration will produce prompt catharsis without absorption. In certain hydremic conditions with edema or with fluid in the peritoneal or pleural cavities, even a concentrated solution is not absorbed. I have the records of one autopsy at the Massachusetts General Hospital. The peritoneal and pleural cavities of this patient contained a small amount of fluid and some fibrin clots, the epithelium in the tubules of the kidney was flattened and the interstitial tissue was edematous; there was no evidence of a glomerulo-nephritis, however. The condition of the kidneys suggested action by some toxic material. We do not know how quickly the salt may be absorbed from the stomach, very little being necessary to cause severe symptoms. Idiosyncrasy must always be considered as a possible factor. I do not believe it wise to give magnesium sulphate in cases of intestinal obstruction; in such cases there is a greater tendency to absorption and the longer the salt remains in the bowel the more will be absorbed.

THE PHYSIOLOGIC ACTION, USES AND ABUSES OF ALCOHOL IN THE CIRCULATORY DISTURBANCE OF THE ACUTE INFECTIONS

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The reputation of alcohol as a cardiac stimulant is as old as our knowledge of medicine. It has been a household remedy for generations and even radical prohibitionists have permitted its use for medicinal purposes. The medical profession in this country have prescribed it freely, and especially in that group of cases under consideration—the acute infections. It has been so securely entrenched in our therapeutic armamentarium that in this country, until very recent years, those who opposed its use in certain acute infections, as pneumonia, were looked on as temperance fanatics. As a preface to the present discussions the therapeutic history of alcohol in Europe during the last century is of interest.

Alcohol was so little used in Germany in the treatment of the acute infections during the middle of the nineteenth century that a physician in Coblentz was held responsible for the death of a typhoid patient for whom alcohol had been prescribed. Shortly after this, Todd, in Dublin, advocated its use in pneumonia and his teachings were quite extensively followed in the British Isles. Somewhat later Binz and his pupils, having demonstrated that alcohol was a food and reduced rather than elevated body temperature, the German clinicians, headed by Von Jurgensen, began using it extensively in febrile conditions. This wave reached its height at the Wies-

baden Congress in 1880, when alcohol was generally lauded as a valuable therapeutic agent in the acute infections. Immediately after this the experimental work of Schmiedeberg and Von Noorden and the clinical experience of Strümpell cast a shadow of doubt over its desirability, and since that time the pendulum has been swinging the other way. This is shown by the lessened consumption of alcohol in some of the large general hospitals in Europe, as, for instance, in the Vienna General Hospital, in which in 1897 $10,000 was spent for alcohol, and in 1905 this had been reduced one-half; and Cabot has shown that there is the same tendency in some of the large general hospitals in this country.

That the amount of alcohol used for medicinal purposes is on the wane does not necessarily prove that it has little value as a therapeutic agent, especially as the change in sentiment has been directly associated with a general prohibition movement.

For our purpose we must approach the subject from a different standpoint, viz.: first, the character and cause of the cardiovascular disturbances in the acute infections; second, the physiologic action of alcohol on the normal mammalian heart; third, the action of alcohol on the cardiovascular apparatus of man and animals suffering from acute infections, and finally, evidence collected from clinical experience.

It is perhaps unnecessary to mention that alcohol has some value as an antipyretic, owing to its inhibitory action in the process of oxidation (von Wendt).[1] Of more importance, and perhaps meriting a word, is its effect in combating the toxemias of the acute infections. There is still considerable difference of opinion on this point, but the recent careful experimental work of Laitinen[2] lends support to the earlier views of Koch and

1. Von Wendt, G.: Ueber die Einwirkung des Alcohol auf die Körper-Temperature des Menschen, Skand. Arch. f. Physiol., 1907, xix, 171.

2. Laitinen, T.: Ueber die Einwirkung der kleinsten Alcoholmenge auf die Widerstandsfähigkeit Thierischen Organismus, etc., Ztschr. f. Hyg. u. Infectionskrankh., 1907-08, lxiii, 139.

Doyen, that even in small doses it diminishes the bactericidal powers of the blood and lessens the animal's resistance to infection.

NATURE OF CARDIOVASCULAR DISTURBANCES

Regarding the nature of the cardiovascular disturbances in the acute infections, the early clinicians recognized the frequency of weak heart, ascribing it to the fever and parenchymatous changes in the heart muscle, first detected and described by Virchow. Somewhat later Hayem called attention to the interstitial changes and the endarteritis and thrombosis of the coronary arteries, this latter accounting for the sudden deaths met with, especially in diphtheria. Romberg was able to demonstrate a progressive acute myocarditis developing some time after the onset of the infection and continuing for some time after its subsidence. Demich attacked the problem from the physiologist's standpoint and discovered that cardiovascular changes analogous to those present in the acute infections could be produced by section of the cord or by vasomotor poisons, such as chloral or chloroform. This led Naunyn[3] to investigate more carefully the clinical signs and symptoms of the cardiovascular apparatus in the acute infections; his results supported Quincke's theoretical views, inasmuch as the ordinary signs of weak heart-muscle, such as faint heart-tone, feeble pulse, arrhythmia and bradycardia were exceedingly infrequent, the clinical findings pointing more to disturbances in the vascular mechanism. Riegel, with the assistance of the sphygmograph and Maragliano[4] with the plethysmograph, confirmed in the main Naunyn's surmise that vasomotor factors were responsible for the disturbance. That functional disturbance of the vasomotor control play an important rôle is further supported by the pathologists, who were often unable to find adequate anatomic changes to account for

3. Von Dubczanski and Naunyn: Arch. f. exper. Path. u. Pharmakol., 1872, i, 181; 1882, xviii, 49.
4. Maragliano: Ztschr. f. klin. Med., 1888, xiv, 309.

the collapse and sudden death. Furthermore, in many of these cases the conditions of the pulmonary and systemic vessels could best be explained by vasomotor paresis. To this evidence was added the effect of the acute infections in animals. Heidenhain, Charrin and Gley, Raczynski,[5] and especially Romberg and Pässler,[6] studied the effect of a number of the more common micro-organisms on the cardiovascular system. These results are so in accord that it is only necessary to refer to a few of the experiments.

Cultures of a streptococcus obtained from a case of scarlatina, when injected into rabbits, produced cardiovascular disturbance, which can best be considered in two stages. Shortly after the injection, a slight and inconstant vasodilatation could be demonstrated, leading to a slight fall in the pressure; later with approaching death the blood-pressure falls, apparently the result of vasomotor disturbances, as the heart's strength is still good, as shown by the prompt rise in blood-pressure following compression of the aorta.

Cultures of the colon bacillus behaved somewhat differently, impairment of the heart being most pronounced. The pneumococcus and diphtheria bacillus behaved in the same manner as the streptococcus, paralyzing the vasomotor center, leading to engorgement of the splanchnic circulation and underfilling of the vessels of the brain, muscles and skin. Involvement of the heart only occurred late, and then apparently secondary to nutritional disturbances caused by the vasomotor paresis. Especially in pneumococcus infections the heart remained intact to the last, this being in accord with the absence of anatomic changes in this organ after death from pneumonia.

It would appear, therefore, from clinical, anatomic and experimental evidence that the circulatory disturbances in the acute infections are chiefly vascular in origin, the heart being affected to a much less marked degree.

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5. Raczynski: Deutsch. Arch. f. klin. Med., 1897, lxiii, 27.
6. Romberg and Pässler: Deutsch. Arch. f. klin. Med., 1899, lxiv, 652.

ACTION OF ALCOHOL IN MAMMALS

Regarding the physiologic action of alcohol in mammals, the published results would appear to be quite at variance; these apparent differences can, however, be largely explained by the method of administration and especially the dosage. Considering these points and selecting only those experiments where methods of precision have been used, we find that the results are really in accord.

A weak solution of alcohol 0.13 to 0.3 per cent. transfused through the mammalian heart has a stimulating effect. The strength of the solution necessary to bring about a certain effect cannot be fixed absolutely. Generally speaking, however, dilutions below 0.13 per cent. are inactive and above 0.3 per cent. act as a depressant. Computing the amount of blood in man as 7 per cent. of the body weight, in order to have the above minimum in the circulating blood, would require about 7 c.c. of absolute alcohol, and for the maximum amount about 15 c.c. of absolute alcohol, or 15 to 30 c.c. of whisky. We must bear in mind that when it is administered by mouth, the delay in absorption would prevent the entire amount ingested from appearing at one time in the circulating blood. When alcohol is administered intravenously to animals, it has been shown that an amount equivalent to 0.1 to 0.3 per cent. in the circulating blood raises blood-pressure and increases the systolic output without necessarily increasing the pulse frequency (Dixon,[7] Rosenfeld,[8] Hasovec,[9] Kochmann,[10] Wood and Hoyt[11] and Bachem[12]). This rise in pressure is rather transitory, ranging from two to twenty minutes. When larger doses are given, all agree that alcohol acts as a

7. Dixon: Jour. Physiol., 1906-07, xxv, 346.
8. Rosenfeld (referred to by Bachem): Centralbl. f. inner Med., 1907, xxviii, 849.
9. Hasovec: Wien. Med. Wchnschr., 1901, lix, 457.
10. Kochmann (referred to by Heinz): Handbuch der expermentellen Pathologie u. Pharmakologie, 1905, i, 985.
11. Wood and Hoyt: Univ. Penn. Med. Bull., 1905-6, xviii, 70.
12. Bachen: Centralbl. f. inn. Med., 1907, xxviii, 849.

depressant. One point of considerable significance is that it is impossible to determine beforehand in any given animal either the minimum or maximum amount required for a stimulating action.

There is still considerable difference of opinion in regard to the cause of the rise in pressure after moderate doses. Whether due to direct stimulation of the heart, the direct effect on the vessel walls, or the effect on the vasomotor center has not been definitely determined. It is certain, however, that large doses of alcohol paralyze the vasomotor center.

CLINICAL EVIDENCE

The clinical evidence relating to the value of alcohol in the acute infections may be divided into two classes, one statistical and of personal impressions, the other careful bedside study, with measured amounts of alcohol, and determination of changes in systolic and diastolic pressure, pulse-rate, etc.

Regarding the value of statistical evidence, it is only necessary to glance back over the therapy in pneumonia during the past fifty years. Laennec believed that he had a specific in tartar emetic; the advocates of venesection had their day and it was only after Skoda demonstrated that the mortality was just as low or lower when bleeding was not used, that the profession discontinued it as a general measure. The supporters of both of these measures furnished statistics that possessed the appearance of evidence. Petrescu treated 2,215 patients with pneumonia with large doses of digitalis, with a mortality of only 1.7 per cent. Aufrecht reported a mortality of 2.6 per cent. in a series of 379 cases, treated with quinin hypodermically. Results equally favorable have been reported after aspirin, creosote and iodids in large doses.

It would appear that, if purely statistical evidence were all that was required to establish a therapeutic fact, there is here sufficient proof. The error lies in the manner in which the statistics have been collected. The mor-

tality of pneumonia is largely dependent on the age of the individual, his previous habits, the severity of the epidemic and the stage of the disease in which he comes under observation. Petrescu used his digitalis treatment on recruits—all young and healthy men—in whom the mortality would naturally be low, as Risell by pure symptomatic treatment reported a mortality of only 1.8 per cent. in 127 patients between the ages of 20 and 30 years. Statistics bearing on the value of alcohol in the treatment of acute infections are too few to permit drawing conclusions, even if free from the objections referred to. Dr. John Hay divided a series of pneumonia patients into two lots by assigning every other patient to one group. Those treated without alcohol showed a mortality of 29.5 per cent.; those receiving alcohol 45.5 per cent. We have heard a great deal of the low mortality from pneumonia in the London Temperance Hospital, but the total number treated is too small to provide evidence.

A more accurate method of approaching the problem is to determine carefully the effect of alcohol on normal individuals and those suffering from the acute infections, and if possible the effect on infected animals. With our present means of taking blood-pressure and estimating the systolic output, we are in a position to determine with a fair degree of accuracy the action of alcohol on the cardiovascular apparatus of man.

A limited number of observations of this character have already been made, and although the results are somewhat at variance, as are the results of these same studies on the hearts of the lower animals, these differences can be explained largely by the dosage and the peculiarity of alcohol, that in the same amounts it does not always affect the cardiovascular apparatus in the same manner.

Studies on normal man show that he reacts to alcohol in the same manner as the lower animals. When given in such quantities that the amount in the circulating

blood is not greater approximately than 0.15 per cent., or about 6 c.c. of absolute alcohol, little if any effect on the cardiovascular apparatus can be observed. When the quantity given is equivalent to from 0.15 to 0.3 per cent. in the circulating blood, equal to 6 to 12 c.c. of absolute alcohol, there is as a rule evidence of cardiovascular stimulation, as there appears, after a lapse of fifteen to twenty minutes, a moderate rise in blood-pressure, varying from 10 to 20 mm. (Kochmann, Binz, Wiesenfeld). A larger amount, equivalent to 40 c.c. of absolute alcohol, invariably acts as a cardiovascular depressant. Some investigators have been unable to detect a rise in blood-pressure, even with moderate doses (Cabot, Crile). The great difficulty in both animal and man is to determine in any single individual either the minimum or maximum amount required for a stimulating action.

In this respect it differs from other cardiac tonics, as with digitalis, for instance, we may be certain that a given amount will affect the mammalian heart in a characteristic manner. For this reason alcohol must always be an unsatisfactory therapeutic agent, as a remedy which in moderate doses may or may not have the desired effect, and which in somewhat larger doses develops an unfavorable action, is not to be relied on in an emergency.

Regarding the cause of the rise in blood-pressure following moderate doses, Dixon and Kochmann consider it due to constriction of the splanchnic vessels, the associated dilatation of the peripheral vessels failing to compensate for the splanchnic constriction. Wood and Hoyt confirmed this view, as they have shown by means of the plethysmograph that the peripheral vessels were dilated during the rise in blood-pressure, and inasmuch as the pulse-rate was not materially changed it could best be explained by constrictions of the splanchnics. This constriction of the splanchnic vessels, according to Dixon and Kochmann, is due to stimulation of the vasomotor center.

Some work has already been done on the effect of alcohol on the heart of animals suffering from acute infections. Pässler in the course of his extensive experiments on the nature of the cardiovascular disturbance in the acute infections used alcohol, caffein, camphor and digitalis in order to determine their action under these conditions. The effects of alcohol in a few instances were favorable, but in the majority of trials simply increased the vasomotor paresis, which Pässler determined was the most important circulatory disturbance in the acute infections.

The effects of caffein and camphor were uniformly favorable. Dennig,[13] Hindelang and Grünbaum gave infected dogs alcohol by mouth in a dosage equivalent to 6 c.c. of absolute alcohol in man, and noted after five minutes a very transitory rise in pressure, followed by a fall which persisted for forty-five minutes. When larger doses were given equivalent to 20 c.c. of absolute alcohol in man, the primary rise in pressure did not develop, but from the beginning the effect was a depressing one.

Carefully conducted studies on the effect of alcohol in the acute infections in man have recently been conducted by Dennig, Hindelang and Grünbaum.[13] The care with which these observations have been made render them more convincing than the entire mass of conflicting, inaccurate clinical reports.

Patients were selected who were not addicted to the use of alcohol, and the systolic and diastolic blood-pressure and pulse-rate were observed for a period of one or more hours after the administration of the alcohol. This series of studies included sixty-two febrile patients, the majority acute infections. The test was applied to successive groups of patients, each receiving larger amounts of alcohol. The first group of ten, including three pneumonia patients, received, well diluted, an equivalent of 6 to 10 c.c. of absolute alcohol. In all but three cases there

13. Dennig, Hindelang and Grünbaum: Deutsch. Arch. f. klin. Med., 1909, xcvi, 153.

was a fall in both systolic and diastolic pressure, and the systolic output, as determined by the product of pulse-pressure by pulse-rate, was reduced. This period of cardiovascular depression continued for one and one-half to two hours.

The second group, consisting of nine patients, including five suffering from pneumonia, received from 11 to 20 c.c. Two pneumonia patients reacted by a slight rise in pressure and increased systolic output; in the remaining seven patients the blood-pressure fell and the systolic output was decreased. The third group, including 25 patients, received, well diluted, an equivalent of 20 to 30 c.c. of absolute alcohol. All but five of these patients gave evidence of the depressing action of the alcohol. Included in the five cases that gave a slight rise in pressure were one pneumonia and one erysipelas. Still larger doses, equivalent to 30 to 40 c.c. of absolute alcohol, were administered to a group of seven febrile patients and all reacted by a fall in pressure and lessened systolic output.

Summarizing this experiment, those patients receiving 6 to 10 c.c., 70 per cent., 10 to 20 c.c., 77 per cent., 20 to 30 c.c., 80 per cent., 30 to 40 c.c., 100 per cent., reacted by a fall in pressure and lessened systolic output. These results on the whole are in accord with those of Cabot, who was unable with varying doses of alcohol to demonstrate in febrile patients a rise in blood-pressure.

The above results, like the animal experiments, impress us with the uncertainty of the reaction of the individual to alcohol; as even in small doses it may, and in large doses invariably does, depress the circulation. It is fair to assume that in these conditions drugs like camphor, caffein and digitalis are of much more value, as they are more constant in their action and much less liable to affect the patient unfavorably.

SUMMARY

In the circulatory disturbances of the acute infections, impairment of the vascular regulating mechanism is

more apparent than active disturbance of the heart, and therapeutic measures should be directed toward the prevention or correction of these vasomotor disturbances. Alcohol in man and the lower animals, when taken in small amounts, frequently acts as a cardiovascular stimulant. The exact method of action is still disputed. Larger amounts of alcohol in individuals not addicted to its use, invariably act as a cardiovascular depressant by paralyzing the vasomotor center. The border-line between the amount acting as a stimulant and the amount having a depressing action is variable, and this variability in action renders alcohol an undesirable therapeutic agent.

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ABSTRACT OF DISCUSSION

Dr. Richard Cabot, Boston: In the use of alcohol in these circulatory disorders there is the difficulty of knowing whether one is dealing with alcohol or with a variety of other substances combined with alcohol in the substance known as whisky. When I began to work with alcohol experimentally I tried to use absolute alcohol and it has been said that the use of absolute alcohol in connection with acute disease is advantageous. So far, I have been unable to get any considerable number of patients to take absolute alcohol, either diluted, flavored or in any other way. They objected so strongly that, in my hands, its use has been impractical. Therefore I have had to use that very uncertain mixture known as whisky and all my results in blood-pressure work with whisky have been, therefore, not properely attributable to the action of alcohol. If anyone has found any way in which he can so flavor absolute alcohol to make patients take it without objection I would like very much to hear of it.

Dr. A. Jacobi, New York: Alcohol is indicated in cases in which sepsis is imminent. There is no better antiseptic than alcohol, no purer antiseptic. I am satisfied with American whisky; it does my work. There are cases of sepsis from diphtheria, for instance, in which the patients may be saved by whisky. I speak of those cases of diphtheria so malignant from the beginning as not to be touched by antitoxin. In such cases no dose is too large; it is impossible to cause alcoholic intoxication until sepsis has disappeared. Alcohol is not indicated while active hyperemia prevails.

THE DIAGNOSTIC VALUE OF THE ORTHODIAGRAM IN HEART DISEASE*

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The orthodiagram has been a disappointment to those clinicians who had hoped to find an accurate estimation of the size of the heart of use in diagnosis. Particularly in the field of cardiac neurosis and early myocarditis, in which the ordinary diagnostic methods fail to show any enlargement, evidence of a slight enlargement might be expected to have diagnostic or prognostic import.

The roentgenogram does not give us such evidence because of the magnification of the cardiac shadow by the divergent rays and because of the lack of definition at the margin, since the heart is in active motion while the exposure is being made. The orthodiagram, however, gives perfectly definite images of a moving organ, allows of the observation of any anomaly of motion, and depends only on the skill of the operator in the interpretation of the images viewed. In addition it leaves a permanent record of that interpretation in the actual dimensions of the organs observed.

Of the various dimensions of the heart shadow which have been proposed, the following have been most commonly adopted:

1. The right-median (M.R.) or greatest perpendicular distance from the right border to the median line (*k-l*).
2. The left-median (M.L.) or similar measurement to the left (*m-n*).
3. The total transverse (T.T.) or sum of M.R. and M.L.
4. The long diameter (L.) measured from the auriculovenous junction to the apex (*a-d*).

* From the Department of Internal Medicine, University of Michigan.

5. The area of the completed heart shadow. A dimension less frequently used is the transverse (trans), measured from the left auriculoventricular junction to the auriculohepatic angle (*b-c*).

M. R. and M. L. are the orthodiagraphic equivalents of the measurements obtained in routine percussion of the deep cardiac dulness, and as such have a distinct value as a check on the examiner's technic. But, because they are always measured in the horizontal direction without

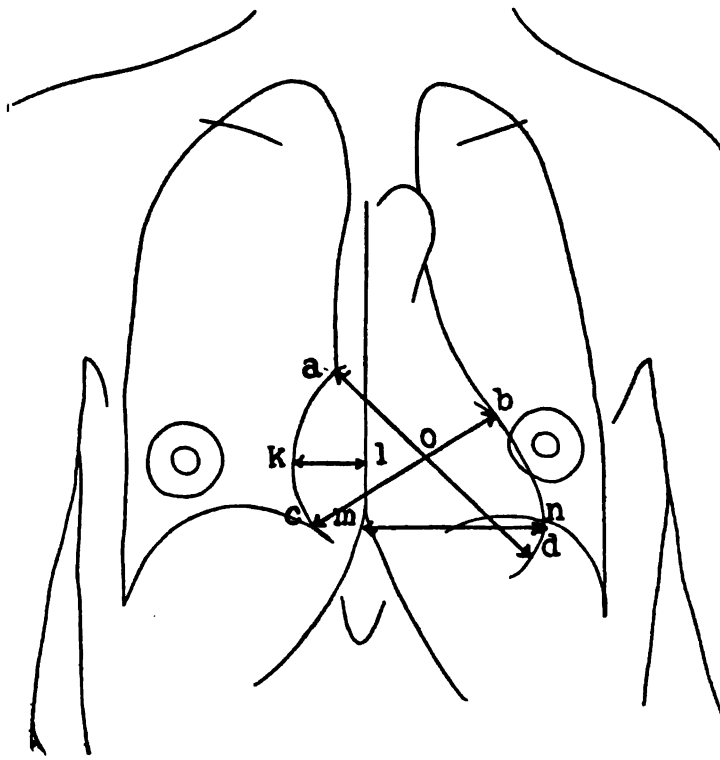

Fig. 1.—Normal orthodiagram showing usual dimensions

reference to the obliquity of the long axis of the heart, their numerical value depends directly on the angle of obliquity, approaching the long diameter with a transverse position, and the transverse diameter with a vertical position of that organ. The sum of the two, therefore, bears no fixed relation to the size of the heart and any conclusions drawn from a comparison of such values must be inaccurate. The transverse diameter

is also an inaccurate criterion, because its right lower extremity is not a fixed point, but depends on the position of the heart with reference to the diaphragm.

The orthodiagram of the heart is never a closed figure (Fig. 3). The outline cannot be followed through the shadows of the sternum and the vertebral column above, or that of the liver below. Before the area can be determined the figure must be completed. This is usually done in

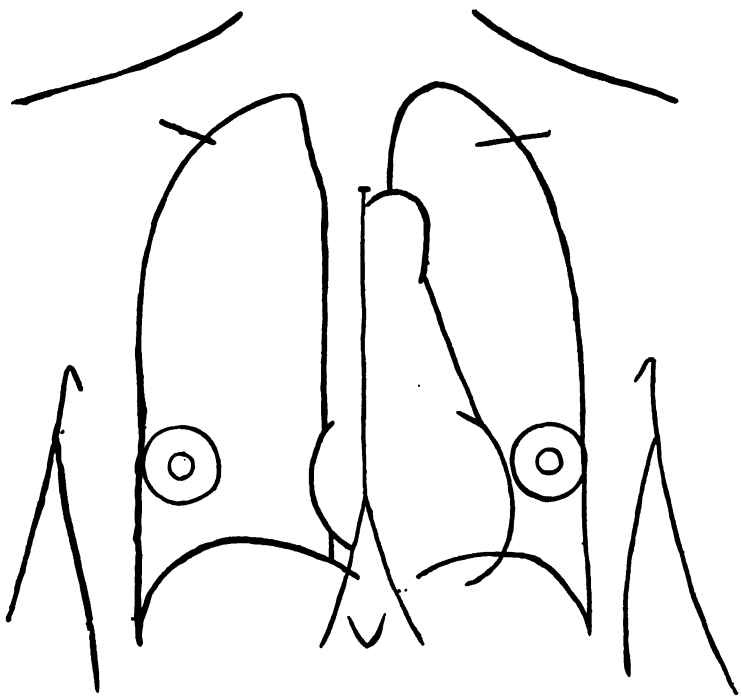

Fig. 2.—Splanchnoptosis, Case 126, M.R. 2.7 cm.; M.L. 7.8 cm.; long diameter 11.5 cm.; area 81 sq. cm.; index .830. Right auricular shadow does not meet the diaphragm shadow. Vertical position.

free-hand, in broad curves to suit the notions of the observer. The upper border usually shows only a short defect and the probable position of the line bridging it is fairly well defined. The lower border is often so deeply sunk in the liver shadow that it is absurd to attempt to supply it. In normal hearts this lower border is a fairly straight line, but pathologic-

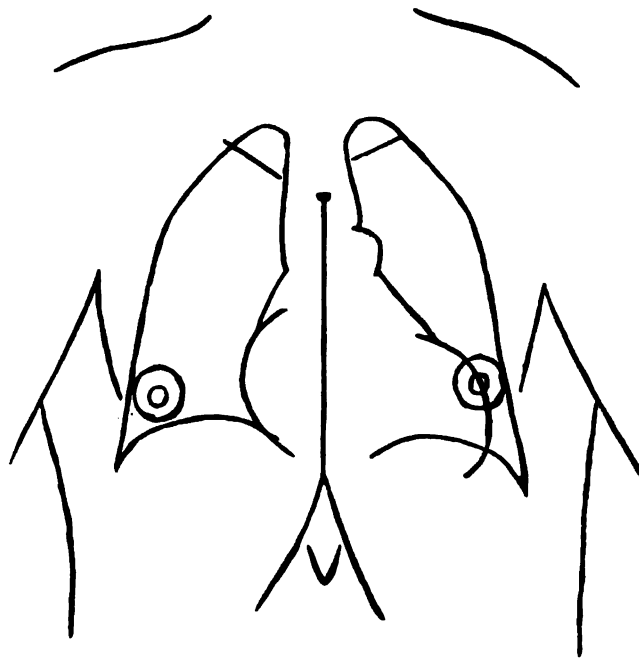

Fig. 3.—Aortic regurgitation well compensated. Snub-nosed heart. Case 58, M.R. 4.5 cm.; M.L. 9.4 cm.; long diameter 14.8 cm.; area 115 sq. cm.; index .378.

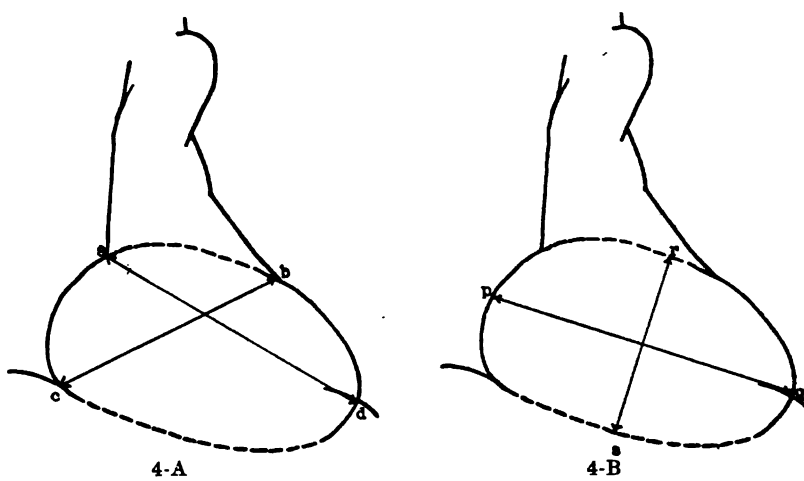

Fig. 4.—Comparison of the usual diameters with those constructed for the estimation of the area by our method.

ally it may become considerably curved. Therefore the completed heart outline represents only the examiner's opinion of its size and shape.

The estimation of the area so enclosed is best accomplished by the use of the planimeter, an instrument used by engineers for measuring irregular areas. Its scientific accuracy is limited only by the exactness with which the circumference can be followed by a needle-point. By the kindness of Professor J. A. Moyer, of the engineering department, we are able to measure all our diagrams by this means.

One may assume that the heart shadow approximates an ellipse and apply the formula for the area of this surface, namely, 3.1416/4 times the product of the long axis and the short axis. By drawing the longest diameter (*p-q*) of the completed figure, then constructing a short diameter (*r-s*) normal to and bisecting this line, and using these values in the above formula, results are obtained which vary but little from the planimeter values (Fig. 4). This longest diameter (*p-q*) is not the same as the "long diameter" (*a-d*) above described. The latter is drawn from the auriculovenous angle and is frequently considerably shorter than a line drawn from some other point on the right border. To make the approximation closer, this line should be drawn as near the center of inertia of the figure as possible, although, actually, it often lies a short distance above it. The average error of the method in our series is in the neighborhood of 3 or 4 per cent. and the highest was 8 per cent. in a heart of very irregular shape.

Clayton[1] has proposed a method of approximation based on a similar calculation using the long and the transverse diameters. In a series of normal diagrams he found 70 per cent. of the product of these dimensions closely approximated the area. The two diameters intersect at such an angle that the transverse diameter always exceeds in length a perpendicular to the long diameter, thereby reducing the necessary constant factor from 0.7854 to 0.7000. The difference in length depends, however, on the obliquity of this angle, which in pathological hearts is subject to wide variation, resulting in a considerable error in the majority of cases.

Before slight enlargements of the heart or changes in its position can be recognized, a standard or norm must be established. Series of measurements of normal hearts have been published by Dietlen,[2] Groedel[3, 4]

1. Claytor and Merrill: Am. Jour. Med. Sc., 1909, cxxxviii, 549.
2. Dietlen: Deutsch. Arch. f. klin. Med., 1906, lxxxviii, 55.
3. Groedel, F. M.: Die Orthoroentgenographie, Munich, 1908.
4. Groedel, F. M.: Roentgen Diagnostik, Lehmann's medizinische Atlanten, vii, Munich, 1909.

Claytor, and others. The tables of Dietlen[2] were chosen for use in the University Hospital, because the number of cases reported and the number of observations on each case are larger than in any of the others. It includes the measurements of 187 male and 74 female adults, classified according to age, weight, stature, etc. In his opinion, the dimensions follow weights rather more closely than any other one factor, and the table for adult males classified by weights was accordingly selected for a standard and is shown in Table 1.

TABLE 1.—TABLE OF DIMENSIONS OF 187 NORMAL HEARTS, AFTER DIETLEN

			Ttl. Trs. Diam. (mm.)			Long. Diam. (mm.)			Area (Sq. cm.)		
Class.	Kilos.	Pounds.	Max.	Aver.	Min.	Max.	Av.	Min.	Max.	Av.	Min.
I	40-44	88-97	123	113	106	135	121	114	104	92	78
II	45-49	100-108	122	114	110	141	129	126	112	102	98
III	50-54	111-120	138	124	107	150	135	120	124	104	84
IV	55-59	120-132	147	129	114	151	140	128	128	112	101
V	60-64	133-134	146	131	104	159	141	127	138	114	91
VI	65-69	145-146	145	132	123	152	145	134	133	118	102
VII	70-74	157-165	149	134	122	162	148	135	149	122	106
VIII	75-79	166-175	150	145	131	161	155	136	139	131	120
IX	80-84	176-184	153	145	139	156	153	150	134	133	124

The use of this table has been found unsatisfactory. The average values appear to be too large for our cases in every class, from light weight to heavy weight. The position of the patient may be to blame for some of this, since Dietlen used only the dorsal position, while many of our orthodiagrams were taken in the erect position. A factor which is probably more important is the sort of material he used, much of it being drawn from soldiers from a neighboring military post, men who are kept in training by systematic and strenuous physical exercises, and may be expected to show hearts unusually large for their weight. Possibly also racial characteristics of build and the proportion of thorax to abdomen materially alter the obliquity of the heart's axis, and so the proportions.

Both Groedel and Claytor find somewhat smaller values on diagrams taken in the vertical position, but their series are rather too small to allow of conclusions.

A more serious obstacle to the estimation of hypertrophy is the wide variation of individual cases from the "average normal," as shown by the maximum values in any class. Naturally the greater the number compiled under any one class, the greater the liability of finding one very large and one very small heart. So we see the greatest variation in Class V, which includes thirty-four individuals, or fifteen more than the next largest class. Here the total transverse diameter reaches a maximum of

14.6 cm. with a minimum of 10.4 cm., a difference of 4.2 cm., a variation of 32 per cent. on the average of 13.1 cm. On the area the maximum reaches 138 sq. cm., with a minimum of 81 sq. cm., a difference of 47 sq. cm., or 41.2 per cent. on the average of 114 sq. cm.

The "normal average" can be of comparatively little use in the question of a pathological increase in the heart size. A given heart must be judged against the maximum which is normal for that class. Judged by these standards, we find that some hearts which are undoubtedly hypertrophied as the result of valvular disease or nephritis, do not exceed the maxima, nor is it possible to demonstrate enlargement in hearts which

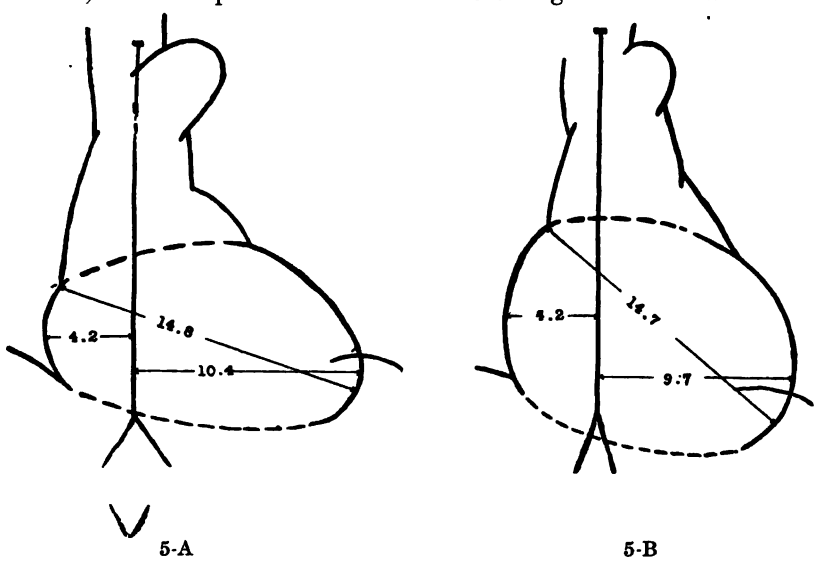

Fig. 5.—Showing the unreliability of the conventional linear dimensions. The smaller diagram has equal and larger dimensions than the larger one to the right. The latter is hypertrophied from an old mitral regurgitation.

from a clinical point of view are manifestly insufficient. We need a more definitely established normal, with a critical study of any and all cases approaching the maxima, and excluding all cases that are clinically open to the suspicion of abnormality of any sort. From our observations it is not at all impossible that the large class of neurasthenics may have large hearts and it would seem advisable to exclude such from the list. Extremely shallow and extremely deep thoraces may also be excluded, on the ground that the depth of the mediastinal space may influence the

surface presented to mensuration. The intimate relationship between the inclination of the heart and its dimensions suggests that either its angle should be measured, or some set of dimensions excluding or including this factor should be devised.

Most of the above points are illustrated in the comparison of the two hearts shown in Figure 5. Figure 5-A is from a case of arteriosclerosis with anginoid symptoms. Its dimensions are: M. R., 4.2 cm.; M. L., 10.4 cm.; T. T., 14.6 cm.; long diameter, 14.8 cm.; area, by planimeter, 100 sq. cm. The averages given by Dietlen for men of his weight are as follows; T. T., 13.4 cm.; long diameter, 14.8 cm.; area, 122 sq. cm. Figure 5-B is from a young adult having a mitral regurgitation follow-

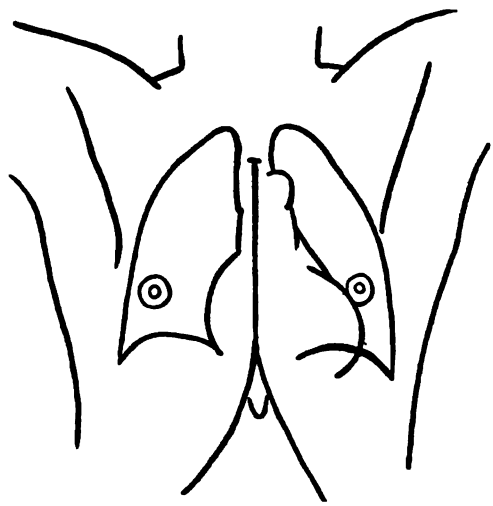

Fig. 6.—Mitral regurgitation, typical "round" heart. Case 96. M.R. 4.2 cm.; M.L. 9.7 cm.; long diameter 14.7; area 121; index .834.

ing scarlet fever in his eighth year. Except for a chronic bronchitis, the patient has no symptoms at present. The dimensions are as follows: M. R., 4.2 cm.; M. L., 9.7 cm.; T. T., 13.9 cm.; long diameter, 14.7 cm.; area, by planimeter, 121 sq. cm. Dietlen's values for his class are T. T., 14.5 cm.; long diameter, 15.5 cm.; area, 131 sq. cm., with a minimum of 120 sq. cm. Here is a heart which is certainly hypertrophied from a clinical point of view, yet all its linear dimensions are smaller than that of a heart which has an area 20 per cent. smaller. Moreover, its area exceeds Dietlen's minimum dimensions by only 1 sq. cm., while it lies

10 sq. cm. below the normal average and 18 sq. cm. below the normal maximum (see Class VIII of Table 1).

Groedel[5] asserts that valuable information may be obtained by the careful analysis of the component arcs of the two heart borders, thereby judging of the relative hypertrophy or dilatation of the anatomical subdivisions represented by these arcs. This principle is accepted by nearly all orthodiagraphists at the present time. Several characteristic shadows are recognized, of which the most typical are the "round heart" (Fig. 6), of mitral disease and the "snub-nosed" heart or "shoe-shaped" heart of aortic disease. Neither of these is pathognomonic of their respective lesions, but each materially assists in the diagnosis of doubtful cases. The altered shape is often the only evidence of the relative severity of two combined lesions, or the only suggestion of the secondary character of the one or the other. It may be noted from the examples given how closely the heart of nephritis approaches that of aortic regurgitation in many cases (see Figures 3, 10 and 11).

It was felt that a numerical expression of the shape of the heart silhouette would be of assistance in the study of such combined lesions and of cardiac changes which were not secondary to valvular disease. For this purpose, there are only four available fixed landmarks on the circumference of the heart shadow (Fig. 1), namely, the right auriculovenous junction (*a*), the auriculohepatic angle (*c*), the upper extremity of the left ventricular border (*b*), and the apex of the heart (*d*). With good illumination these landmarks may be fixed in the majority of cases, especially in the erect position, which is the position chosen in our work. In this position the diaphragm rests at a lower level and the apex of the heart can be more easily followed through the liver shadow. For comparable results it is of course necessary to use a uniform technic.

Of these landmarks, *a* and *b* represent definite anatomical points and will vary in position as the auricles vary in distention and size. In normal cases, *b* usually represents the junction of the conus arteriosus and the ventricle, but in enlarged hearts the left auricle frequently presents, and it then represents the junction of its shadow with that of the ventricle. Point *c* varies with a number of conditions, such as the degree of dilatation of the right auricle, changes in the obliquity of the cardiac axis, lengthening of the arch of the aorta, elevation of the dia-

5. Groedel, F. M.: Deutsch. Arch. f. klin. Med., 1908, xciii, 79.

phragm from abdominal distention or its depression in emphysema, splanchnoptosis, and so forth. The apex (*d*) is the most important of the four, because on its position depends the value of the long diameter and the area. It is also the most difficult to fix exactly. It represents the thinnest part of the heart; its motion has the widest excursion; and it lies depressed beneath the diaphragm shadow in the shadow of the left lobe of the liver. It is perhaps the least reliable of all.

By joining *a* and *d* we have the ordinary long diameter. The line *b-c* represents the transverse diameter as measured by Moritz. These two lines intersect at an oblique angle at 0, the obliquity depending on both the shape and the position of the heart.

The line *b-c* does not accurately represent the auricloventricular septum either in position or in direction, but it may be assumed that the two areas into which the heart shadow is so divided are roughly representative of the auricular and ventricular areas, and, if the two segments are similar with a common base and the obliquity of the axis equal, the areas will be in proportion to the fractional diameters *a-o* and *o-d*, and the ratio $a : o :: o : d$ will roughly represent the surface relations of the auricles and ventricles. Since distention of the auricles is a marked feature in a mitral lesion, the ratio should be larger than normal with mitral disease, and, since hypertrophy and dilatation of the ventricle bear a similar relation to an aortic lesion, it should be smaller in this condition.

Although the assumptions of the previous paragraph are scarcely justified by the conditions, it so happens that most of the errors tend to exaggerate the difference in ratio in the two classes of cases and we believe that the tables shown justify the acceptance of this ratio as an index of the heart form on empirical grounds alone. We have selected from the 170 orthodiagrams available all those which are technically satisfactory, which show definite enlargement and which have an adequate clinical diagnosis.

Our series of normal orthodiagrams is too small to allow of deductions. The indices of the few cases we have observed range between 0.534 and 0.704, but it is probable that the ratio is less fixed in normal than in pathological cases, because the greater mobility of the heart results in variations in the point *c*.

Our results have been tabulated according to conditions, the uncomplicated cases being separated from those showing such complications as

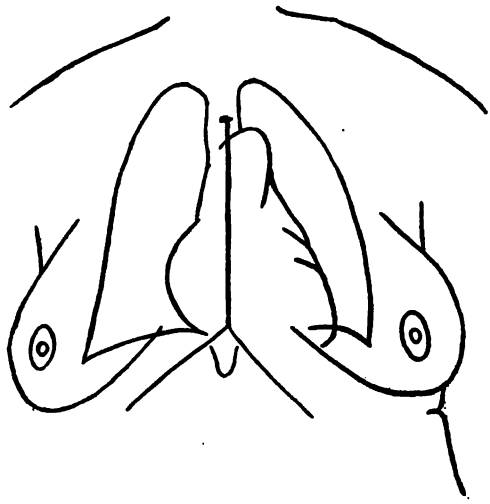

Fig. 7.—Mitral stenosis, showing prominence of left auricular shadow, with low position of the l. auriculoventricular junction. Case 97. M.R. 5.2 cm.; M.L. 9.0 cm.; long diameter 15.1 cm.; area 119; index 1.030.

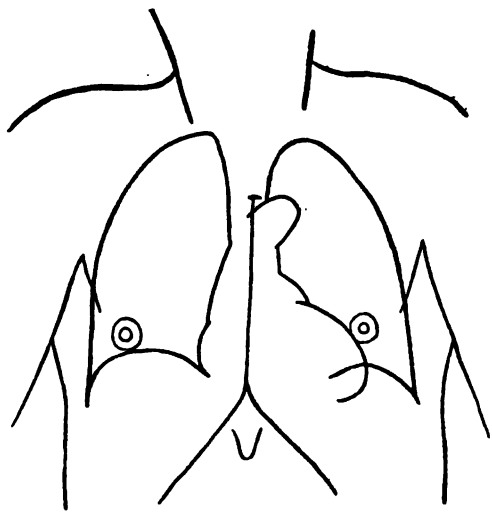

Fig. 8.—Arteriosclerosis. Prominent arch and transverse position. Case 99, M.R. 4.2 cm.; M.L. 10.4 cm.; long diameter 14.8 cm.; area 100; index .386.

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might have some bearing on the shape of the heart, and the latter complications are noted in the last column.

It will be seen that all cases of mitral stenosis show an index in excess of .880, even in the presence of a complicating mitral regurgitation and irrespective of the degree of enlargement. This high value is due in part to the low position of the point *b*, because of the enormous enlargement of the left auricular shadow. This form of heart shadow is very striking and is almost pathognomonic of mitral stenosis.

The clinically uncomplicated mitral regurgitants range from 0.657 to 0.834 (Fig. 6). The two cases complicating nephritis have a value of

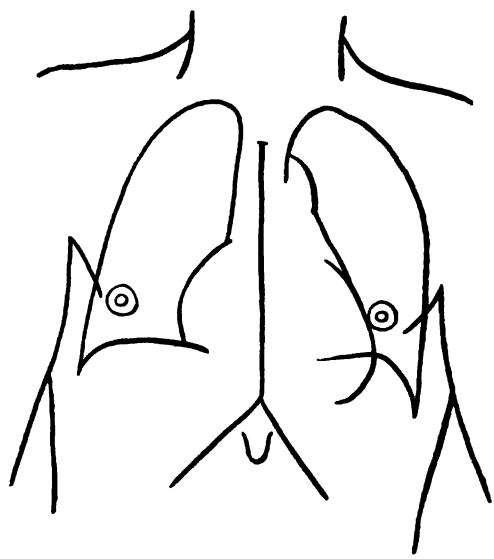

Fig. 9.—Chronic parenchymatous nephritis, mitral regurgitation, typical round heart, both following scarlet fever. Case 100. M.R. 6.8 cm.; M.L. 9.5 cm.; long diameter 16.8 cm.; area 172 sq. cm.; index .711.

0.815 and 0.822, respectively; three cases combined with mitral stenosis exceed 1,000 while one case of mitral regurgitation and aortic regurgitation shows a value of 0.420, placing it more nearly with the latter condition.

Only one case of uncomplicated aortic regurgitation came under our observation and gave an index of 0.378 (Fig. 3). Of the cases showing higher than 0.400, one was complicated with pernicious anemia, and the

other three showed well-marked mitral murmurs, probably as a result of dilatation. Two of the latter are also classified under the nephritics and show the largest areas in our series.

The class of arteriosclerotics is so poorly defined that only the most marked cases are noted. The index ranges between 0.282 and 0.393, with one exception (No. 84), which showed a perpetually irregular pulse, and this is held to account for the value of 0.492. The explanation of the low value in these cases is probably the low and transverse position of the heart (Fig. 8), due to the lengthening of the arch of the aorta. The

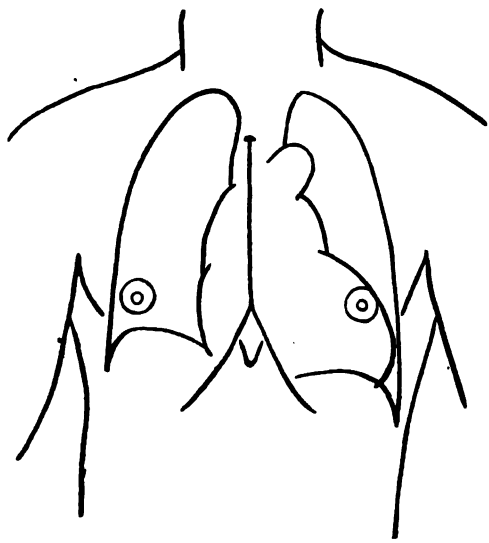

Fig. 10.—Chronic interstitial nephritis, signs of aortic regurgitation. Snub-nosed heart. Case 95. M.R. 4.4 cm.; M.L. 12.2 cm.; long diameter 17.7 cm.; area 177 sq. cm.; index .479.

result is to bring the point *c* higher up on the right auricle. The closely related group of angina pectoris shows similar relations.

Under the head of "myocarditis" have been grouped all the cases of cardiac failure without obvious lesions. Because of the difficulty of diagnosis, the number was limited to these five cases, although this probably represents only a small fraction of the total number. Two showed the permanent type of irregularity and two others are classified with the

nephritics. The lowest value was found in the latter complication with relatively little insufficiency of the heart.

The group of nephritics shows a wide range in index as well as in area. We are not in a position to offer any interpretation of this variability. In a general way we find the cases with cardiac complaints at the lower end of the scale and those complaining of headaches, loss of vision, gastric complaints, etc., near the upper end.

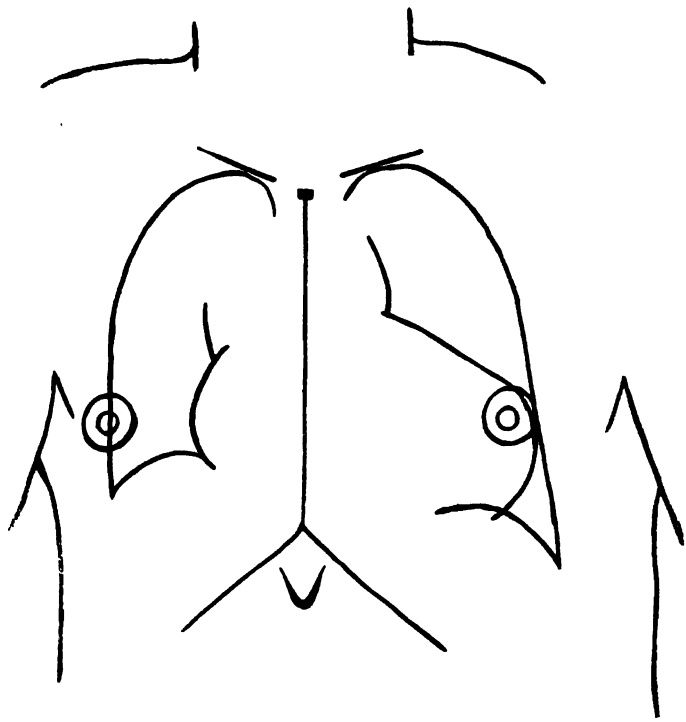

Fig. 11.—Chronic interstitial nephritis. Cardiac failure. Case 59. M.R. 6.1 cm.; M.L. 13.3 cm.; long diameter 19.3 cm.; area 186 sq. cm.; index .280.

The athletes were taken from long-distance runners and range well above the average, lying between 0.731 and 0.912. Casual inspection of the orthodiagram shows a pyriform shadow with a long and wide right auricular border on a comparatively transverse heart. The areas of these figures are all well within the maxima given by Dietlen.

As representatives of the heart form described as the pendulous heart, we have listed five cases of splanchnoptosis (Fig. 2). These hearts are all small, falling near or below the minima for their class. They are characterized by a very low position of the point *c*. Indeed, the auricular border may meet the vertebral shadow above the diaphragm so that the heart appears to be freely suspended above the diaphragm. In such case *c*, as defined above, does not exist and the meeting of the right border with the vertebral border must be taken as the lower extremity of

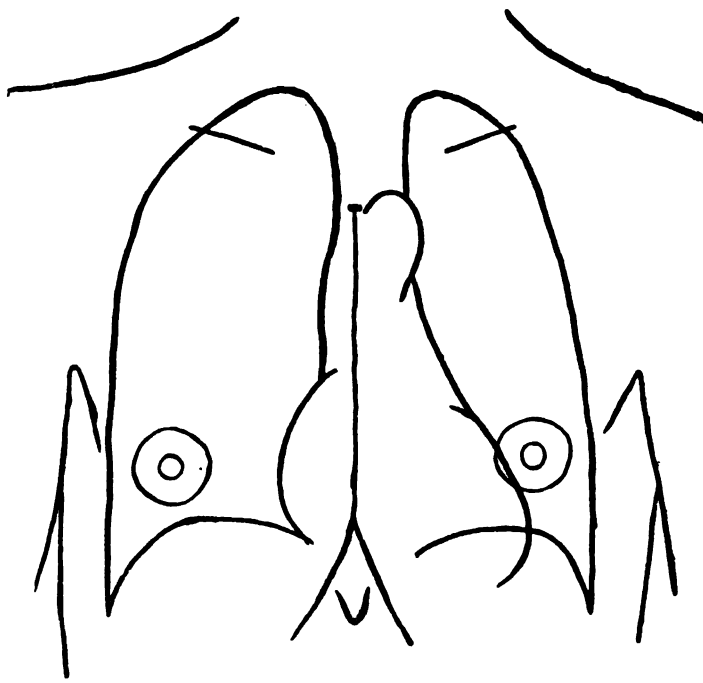

Fig. 12.—Athletic heart. Two-mile runner. Case 142. M.R. 5.3 cm.; M.L. 8.5 cm.; long diameter 14.5 cm.; area 98 sq. cm.; index .735.

the transverse diameter. The index accordingly ranges above 0.816. We believe that this high value may be taken as demonstrating that the thoracic viscera partake of the general relaxation and ptosis found in this remarkable condition.

Although our series of sixty cases is too small to allow of any but the broadest generalizations, we believe that we are justified in the con-

clusion that an abnormal index is an early evidence of the increase in size of one or more chambers of the heart and may occur before such increase can be demonstrated by other means; that a decrease in the index results from left ventricular hypertrophy and dilatation, and an increase indicates a dilatation of the auricles with or without hypertrophy of the right ventricle. In combinations of these two antagonistic factors the index will depend on the predominance of the one or the other (Fig. 13). The wide variation shown in valvular diseases should make

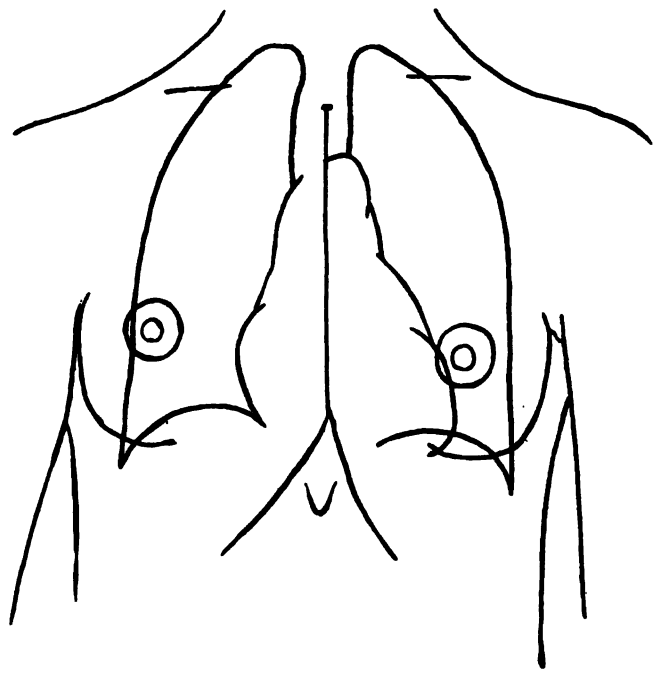

Fig. 13.—Diagram of a case showing a presystolic roll at the apex and a diastolic blow in the third left interspace. Pulse quick but not collapsing. The orthodiagram shows the form and index of mitral stenosis as against aortic regurgitation with an Austin Flint murmur. The latter lesion is either absent or must be insignificant. Case 170. M.R. 5.3 cm.; M.L. 7.2 cm.; long diameter 13.6 cm.; area 96 sq. cm.; index 1,000.

the index valuable in the diagnosis of doubtful or combined lesions, and it is hoped that the smaller fluctuations found associated with renal conditions may sometime be of diagnostic and prognostic value.

TABLE 2.—TABLES OF DIMENSIONS OF 60 ORTHODIAGRAMS CLASSIFIED ACCORDING TO DISEASES

Case.	Index.	Sex.	Age.	Weight.	M.R.	M.L.	Trans.	Long.	Areas. Planimeter.	Areas. Clayton's Est.	Areas. Author's Approx.	Complications.
							MITRAL STENOSIS UNCOMPLICATED					
21	990	F.	..	150	53	95	120	159	136	135	128	
139	1000	F.	48	145	45	82	111	128	81	99	77	
97	1030	F.	53	180	52	90	125	151	119	132	114	
							MITRAL STENOSIS—COMPLICATED					
170	1000	F.	28	128	53	72	110	136	...	105	96	Mitral regurg.
145	1040	F.	..	...	53	82	117	137	108	112	107	Mitral regurg.
60	1110	F.	22	130	46	96	105	150	113	111	110	Mitral regurg.
46	685	M.	60	125	68	90	130	173	141	157	133	Perm. irreg'ty.
							MITRAL REGURGITATION—UNCOMPLICATED					
120	657	F.	..	158	72	110	161	183	171	206	158	
47	690	M.	17	120	53	78	113	143	124	113	123	
57	706	F.	16	118	38	86	115	132	91	107	89	
55	714	M.	28	125	50	98	115	130	103	105	107	
31	781	F.	20	128	46	74	106	130	86	97	84	
96	834	M.	26	170	42	97	122	147	121	127	122	
							MITRAL REGURGITATION—COMPLICATED					
49	420	M.	53	118	66	115	143	183	160	183	167	Aortic regurg.
76	815	F.	53	106	30	95	109	135	108	103	110	Nephritis.
100	822	M.	22	185	68	95	148	168	172	174	169	Nephritis.
26	936	F.	17	90	38	77	98	127	82	86	84	Splanch'tosis.
170	1000	F.	28	128	53	72	110	136	...	105	96	Mitral stenosis.
145	1040	F.	..	...	53	82	117	137	108	112	107	Mitral stenosis.
60	1110	F.	22	130	46	96	105	150	113	111	110	Mitral stenosis.
							AORTIC REGURGITATION					
58	378	M.	26	127	45	94	108	148	115	112	112	
							AORTIC REGURGITATION—WITH COMPLICATIONS					
87	319	M.	62	136	33	117	113	152	107	121	104	Arterioscl'sis.
88	355	M.	52	136	61	132	161	205	211	231	208	Nephritis.
49	420	M.	53	118	66	115	143	183	160	183	167	Mitral regurg.
11	448	M.	61	126	50	107	112	177	...	...	...	Pernic. anemia.
78	466	M.	48	140	56	124	136	175	[150?]	166	...	Nephritis.
95	479	M.	..	154	44	122	133	177	177	164	170	
							ARTERIOSCLEROSIS					
80	282	M.	60	150	47	87	104	141	105	102	102	
143	336	M.	55	138	34	84	100	119	91	85	94	
118	393	M.	52	156	45	67	105	131	83	96	83	
							ARTERIOSCLEROSIS—COMPLICATED					
87	319	M.	62	136	33	117	113	152	107	121	104	Aortic regurg.
99	386	M.	62	138	42	104	110	148	100	114	101	Nephr. angina.
84	492	M.	71	...	36	96	98	144	100	99	101	P.I.P.

Nephritis—Uncomplicated

59	280	M.	61	177	61	133	132	193	186	177	181	
77	304	M.	..	...	40	110	118	160	118	131	116	
68	445	M.	49	188	58	121	128	188	...	...	...	
74	454	M.	..	...	40	120	110	193	136	148	144	
43	482	M.	56	126	40	118	108	165	114	126	109	
61	564	M.	..	...	38	93	116	133	101	108	101	
37	564	M.	57	125	58	69	109	136	92	103	88	
168	610	M.	53	103	40	108	129	161	...	140	139	
158	728	M.	48	114	43	88	112	142	101	112	100	
154	755	M.	36	152	40	111	120	156	108	131	101	
85	793	M.	51	160	40	83	105	130	90	95	86	

Nephritis—Complicated

88	355	M.	52	136	61	132	161	205	211	231	208	Aortic regurg.
99	386	M.	62	138	42	104	110	148	100	114	101	Arterioscl'sis.
78	466	M.	48	140	56	124	136	175	...	...	...	Aortic regurg.
95	479	M.	..	154	44	122	133	177	177	164	170	Aortic regurg.
69	539	M.	..	...	40	120	119	180	163	150	167	Myoc. insuf.
67	561	M.	45	136	49	93	109	142	98	109	93	Anemia.
42	625	F.	54	134	50	103	120	156	123	131	123	P.I.P.
41	625	M.	64	129	48	134	145	184	164	187	167	P.I.P.
167	750	M.	50	120	43	113	127	162	...	144	138	Myoc. insuf.
76	815	F.	53	106	30	95	109	135	108	103	110	Mitral regurg.
100	711	M.	22	185	68	95	148	168	172	174	160	Mitral regurg.

Angina Pectoris

94	450	M.	51	148	54	78	109	143	117	109	119	
79	495	M.	..	...	60	99	128	164	139	146	138	

Angina—Complicated

99	386	M.	62	138	42	104	110	148	100	114	101	Nephritis.

Myocardial Insufficiency

62	925	M.	..	...	51	137	145	187	163	190	160	

Myocardial Insufficiency with Complications

69	539	M.	..	...	40	120	119	180	173	150	167	Nephritis.
12	688	M.	67	170	48	103	124	152	...	...	...	P.I.P.
167	750	M.	50	120	43	113	127	162	...	144	138	Nephritis.
73	862	M.	32	152	56	106	111	176	162	163	166	P.I.P.

Athletes—Track Team

39	731	F.	24	108	34	84	103	142	100	101	103	
142	735	M.	23	158	53	85	117	145	98	119	92	
141	736	M.	28	123	42	95	113	137	96	109	92	
169	739	M.	22	155	50	84	122	135	...	115	109	
156	768	M.	25	145	48	91	111	144	103	113	100	
149	781	M.	20	142	57	130	147	145	114	113	113	
157	825	M.	22	155	45	95	115	146	101	118	96	
140	841	M.	21	127	36	61	91	117	66	74	71	
146	912	M.	20	132	48	79	118	131	98	109	95	

Splanchnoptosis—Uncomplicated

115	816	F.	32	112	30	62	87	110	63	67	65	
126	830	M.	36	136	27	78	98	115	81	79	79	
2	1035	F.	..	94	47	64	94	112	68	74	72	

Splanchnoptosis—with Complications

23	920	F.	17	102	27	79	83	122	79	71	84	Chlorosis.
26	936	F.	17	90	38	77	98	127	82	86	84	Mitral regurg.

ABSTRACT OF DISCUSSION

DR. SIDNEY LANGE, Cincinnati: Contrary to the reception of most laboratory methods of precision, the use of the orthodiagraph has been received very conservatively, and rightly so, for the orthodiagraphic tracing represents simply the contour of the heart.

We will grant that such an outline tracing does not necessarily give a true idea of the actual bulk of the heart (the same is true of percussion), and even the values obtained by applying the formula of the ellipse, as suggested by Dr. van Zwaluwenburg, may be inexact. We will grant further that, in the majority of the cases, ordinary percussion gives us a fair idea of the location of the heart borders.

Dietlen found in a series of normal adult heart experiments, controlled by the orthodiagraph, that percussion of the right border of the heart was accurate in 89 per cent. of the cases, percussion of the left border was accurate in 78 per cent., while the heart apex was located accurately by the finger in only 69 per cent. But the error of percussion was found to be very small, on the average less than 0.5 cm. This fact does not lessen the value of the orthodiagraphic method, however, for the patients examined were normal ones. Finger percussion may suffice in the average case, but when we are dealing with the obese and emphysematous, and with heart affections complicated by pericardial and pulmonary lesions, percussion may be seriously embarrassed. Percussion, for instance, may show that the cardiac apex is beyond the nipple line, but the orthodiagraph may show that the heart is simply displaced by altered thoracic or abdominal conditions and not enlarged. In other words, the orthodiagraph supplies, as a rule, additional information to that of percussion, which information in cases of doubtful diagnoses may give the clue to a correct solution. It is the supreme court to which obscure cases may be referred.

As a concrete example, suppose in the course of an infectious disease, such as diphtheria, it was desired to determine a very small increase in the size of the heart, the very onset of a myocardial change. The finger cannot always be relied on to detect an enlargement of 0.5 cm.

The finer curves and details of the mediastinal contour, as revealed by the orthodiagraph, cannot be obtained by percussion. These curves and details have much practical significance. They were identified by Dr. La Camp by studies on cross-sections of the chest of a frozen cadaver. By comparative studies of the orthodiagraphic tracings and the clinical and post-mortem findings of a series of cases, their reliability as an index of the changes going on in the heart chambers is striking. In teaching and demonstrating to students, I number the curves 1, 2 and 3 on the left mediastinal border, and 4 and 5 on the right, and I discuss their significance by referring to the numbers.

In arteriosclerosis cases I have obtained, as a rule, a different contour from that shown by Dr. Claytor, the first and third curves (that is, the aortic and the ventricular) being accentuated.

The orthodiagraphic tracing of the mediastinum will frequently reveal abnormal conditions of the thoracic aorta which are difficult of recognition. I refer to simple dilatation and elongation of the aortic arch as evidenced by a prominence of the aortic curve, and more especially to elongation and fusiform dilatation of the descending thoracic aorta, which produces peculiar changes in the orthodiagraphic contour.

The difficulty in determining what the average orthodiagraphic size of the normal heart should be, as brought out by Dr. van Zwaluwenburg, is a real one, but that same difficulty is encountered in the examination of many other organs and functions and does not invalidate the orthodiagraphic method.

I cannot but feel that the practical value of these orthodiagraphic studies is considerable.

Dr. James G. van Zwaluwenburg, Ann Arbor: I heartily agree that the value of the orthodiagram as a check on percussion methods cannot be overestimated. There can be no other check during the life of the patient. Its value in the determination of the outline of the heart is considerable, and often helps in the differentiation of certain valvular lesions. This is recognized by practically every one who has ever used the instrument. But it does not assist in the determination of enlargements of small degree.

Our purpose was to find a numerical equivalent of the shape of the shadow which we could easily apply to the study of doubtful cases, and to the classification of clinical records. As an instance of its value in a doubtful case: one of the last cases I saw was that of a nervous and simple-minded woman, who could give us no helpful history. She had a systolic, a diastolic and a presystolic murmur, without well-marked vascular signs. The diastolic murmur was best heard in the third left intercostal space. The questions arose whether this was an aortic regurgitation with an Austin Flint murmur, or whether there was a mitral stenosis complicating the aortic regurgitation or an unusual transmission of the diastolic murmur of mitral disease uncomplicated by aortic disease. The orthodiagram showed the characteristic shape of mitral stenosis, both by inspection and in the value of its ratio (1,000), leading to the conclusion that the aortic lesion was absent or inconsiderable.

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